"SAFETY AND CLINICAL EVALUATION OF SIDDHA DRUG POONAIKALI VITHAI CHOORANAM IN THE TREATMENT OF AAN MALADU (MALE INFERTILITY)"

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **Preclinical and Clinical study of Siddha drug "PoonaikaliVithaiChooranam" (Internal) in the treatment of AanMaladu (Male Infertility)** is a bonafide and genuine research work carried out by me under the guidance of **Dr.T.Lakshmikantham,M.D(s),** Lecturer**.,** Department of **Maruthuvam**, National Institute of Siddha, Chennai -47, and the dissertation has not formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

Date: **Signature of the Candidate**

Place: Chennai-47 **Dr.K.Rajendran**

CERTIFICATE

This is to Certify that this dissertation work on "**CLINICAL EVALUATION OF SIDDHA DRUG POONAIKALI VITHAI CHOORANAM IN THE TREATMENT OF AANMALADU(MALE INFERTILITY)**" has been carried out by Dr.K.Rajendran Reg No:32141107 during the year 2014-2017 in the Department of Maruthuvam,National Institute of Siddha,Tambaram sanatorium,Chennai-47 under My guidance and supervision in partial fulfilment of regulation laid by the Tamilnadu Dr.M.G.R Medical University,Chennai for the final M.D(Siddha),Branch I-MARUTHUVAM Examination to be held in OCTOBER-2017.This dissertation work is not reprinted or reproduced from any of the previous dissertation work.

PROF.Dr.K.Manickavasakam M.D(s),

Head of the Department ,

Department of Maruthuvam.

CONTENTS

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INTRODUCTION

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Siddha medicine is the oldest medical system developed by 18 Siddhars.The word siddha comes from the word **"SIDDHI**"which means to attain **"PERFECTION OR HEAVENLY BLISS**".

Indigenous medicines including siddha of India are getting much attention nowadays for treating various diseases. This due to their potency and less side effect (Mitchell, 2003). During the past two decade,traditional system of medicine have become a topic of global importance. In south India siddha still remains dominant compared to modern medicine particularly for the treatment of a variety of chronic disease conditions among masses.

In 20th century usage of herbal based medicinal therapy gained importance and found their place in 40% of prescription because of their lesser side effects. on par with other chemical drugs. A remarkable increase in the usage of medicinal plant products in the form of plant extracts and their active components etc.Have been observed in the past decade, among the world population as a primary health care aid.

Yugi muni had done a lot of contribution to the siddha system, includes the classification of disease into 4448. AAN MALADU is one among them. According to Yugi muni in aan maladu the semen exhibits the following characters such as absence of sweetness, buoyancy on water. He further explained the character of urine in aan maldu as froth in urine and symptoms like absence of virility.

Sukkilam one among the seven udal thathukkal is affected in Aan maladu. It can be correlated with male Infertility in modern science . Most cases of male infertility are due to an abnormal sperm count or low sperm motility. Infertility is the inability of a sexually active, non contraception couple to achieve pregnancy in one year. There was a time when infertility was only limited to women. In present scenario male infertility is blamed in 50 % of cases where couples could not conceive naturally. Male infertility is a global problem in the field of reproductive health. .

Infertility bears a social stigma.The incidence of infertility among males 40% females 40% and both sex 20%.

Most of the cases hail from IT back ground, chemical industry, oil refineraries, viral infections at an early age in male child, trauma(testes), endocrine disorder ,low economic status, can also lead to rise in infertility rate. The heat generated from laptops can make an impact sperm production and development making it difficult to conceive down the road. As per WHO guidelines a report with count less than 15 million / ml is oligospermia. The most common problems men face are low sperm count, morphology abnormalities and motility of sperm.

The research study entitled Aan maldu (Male infertility) mainly focus on outcome of qualitative and quantitative analysis of semen in oligospermia patients with the Study drug Poonakali vithai chooranam . Poonaikali vithai chooranam is a polyherbal compound based on the activities of the drug. The Study drug poonaikali vithai chooranam being the poly herbal formulation consists of ingredients possessing anti oxidants (kayakalpha drugs) and aphrodisiac properties.

Since the Study medicine is yet to be documented for its efficacy, it is essential to do safety studies before going for clinical study.

AIM AND OBJECTIVES

AIM AND OBJECTIVES

Aim:

To document the effective Siddha Medicine Poonaikali vithai Chooranam (Internal medicines) in the management of AAN Maladu (male infertility)

Primary Objective:

To evaluate the therapeutic efficacy of Poonaikali vithai Chooranam(Internal medicines) based on Semen analysis in the treatment of AAN Maladu (male infertility)

Secondary Objective:

- To prepare the trail Medicine as per the text Gunapadam Mooligai Vagupu.
  Author: Vaithiya rathinam K.S Murugesa muthalaiyar: 1st Edison pg no 708
  (publication year 1936)
- To collect raw drugs and to get Authentication.
- To evaluate the safety profile of the trial drug in animal models as per
  OECD guidelines -423
- To evaluate the phytochemical analysis of the drug.
- To study the changes in special investigation –Semen Analysis Before and After treatment.
- To evaluate the Infertility Percentage among the study patients with respect to age,occupation, and socioeconomic structure.

REVIEW OF LITERATURE

ஆண்மலடு

"பார்க்கவே ஆண்மகனின் விந்துதானும்

பதமான திதிப்புயில் லாததாலும்

ஏற்கவே சலமீதில் மிதந்ததாலும்

எழிலாக வுயிர்ப்பற்று யிருப்பதாலும்

சேர்க்கவே மூத்திரத்தில் நுரைதான் போலும்

செயலான கருவதுவும் தரிக்கமாட்டா

தீர்க்கவே யூகிமுனி சிகிச்சாரம்

தெளிவாகப் பாடி வைத்தார் திறமிதானே" ***-யூகிமுனி***

The characteristic features of AAN MALADU

The semen in aanmaladu will be devoid of sweetness and life and will float on the surface of water. The urine also will be frothy. Such man will be incapable to impregnate women.

DEVELOPMENT OF SPERM

"உதயத்தில் விந்துவில் ஓங்கு குண்டலியும்

உதய குடிலில் வயிந்தவம் ஓன்பான்

விதியில் பிரமாதி கள்மிகு சத்தி

கதியிற் கரணங் கலைவை கரியே!" ***-திருமூலர்***

In the above verses thirumolar states that the driving force the kundali arises in the sperm which in turn initates the anthakarnanam to bring changes in the ova during fertilization.

5 ARTS OF SPERM

1. Neekal
2. Nelaipithal
3. Nugarvithal
4. Amaithiyakkal
5. Appalakkal

CONFIGURATION OF SEMEN

Based on siddha principles the semen is constituent by eighty drops of blood which is equal to one drop of semen. Therefore wasting a drop of semen is equal to wasting six thousand four hundred drops of blood.

"**அழிகின்ற விந்து அளவை அறியார்**

கழிகின்ற தன்னையுட் காக்கலுந் தேரார்

அழிகின்ற காயத் தழிந்தயர் வுற்றோர்

அழிகின்ற தன்மை யறிந்தொழி யாரோ!"

--- திருமூலர் - பாடல் – 1936

In the above verses states the significance of sperm. In modern correlation spermatogenesis the process by which the male gamete called spermatozoa are formed by various stages like proliferation, growth, maturation, transformation.

SIGNIFICANCE OF SPERM

"விந்து நிலை யறிந்துவுந்து பாயுங்காலம் தேவதாந்த நாதமதுக்கு

யிருண்டாகி சொந்தமுட னேயிரண்டும் ணியுமாகிச் சோதிமணி யானது

விம்பி றையுமாகி வந்தமதிப் பிறையதுவும் வட்டமாகி

வட்டமதி ரண்டுருவாய் மண்ணுமாகி

அந்த முள்ள மண்ணுதற் உப்பாய் நின்றே

யாதியென்ற பொருளான பிண்டமாச்சே"

-அகத்தியர்

After the penetration of the sperm in to the ovum the sperm head fuse with the oocyte to form single cell. Then it undergoes several stage of cell division and finally forms the embryo.

"உன்னிய கர்ப்பக் குழியாம் வெளியிலே

பன்னிய நாதம் பகர்ந்த பிருத்வி

வன்னியும் வாயுவ மாயுருஞ் சுக்கிலம்

மன்னிய சமனாய் வளர்க்கு முதகமே"

-திருமூலர்

The ovum consists of the element earth, whereas the sperm consist of fire and air. The uterine wall which nourishes it ling water and the urine cavity is of the element space. Therefore in the formation embryo of five elements combine and create it.

"**விழுந்தது இலிங்கம் விரிந்தது யோனி**

ஒழிந்த முதல் ஐந்தும் ஈரைந்தோடு ஏறிப்

பொழிந்த புனல்பூதம் போற்றும் கரணம்

ஒழிந்த நுதல் உச்சி உள்ளே ஒளித்ததே!" - ***திருமூலர்.***

At the time of copulation, the semen is ejaculated. The prostatic fluid gives the semen a milky appearance. In the early minutes after ejaculation, the sperm remains immotile, possibly because of the viscosity of the coagulum. As the coagulum dissolves the sperm become highly motile.

"**ஆண்மிகில் ஆண்ஆகும் பெண்மிகில் பெண்ஆகும்**

பூண்இரணடொத்துப் பொருந்தில் அலி ஆகும்

தாண்மிகும் ஆகில் தரணி முழுதாளும்

பாணவ மிக்கிடில் பாய்ந்ததும் இல்லையே. -***திருமூலர்***

At the time of copulation if the male dominates then it is male & if the female dominates then it is a female child. If the male and the female are equal then the child will be neutral gender or a eunuch. Here male indicates the vindhu and the female indicates nadham.

"**வேர்க்கவே வேலிபோல் வளைந்து காக்கும்**

விந்துவுடன் பிராணவாயு விளக்கலாமே" -***யூகிமுனி***

Abana stays outside of uterus and the prana goes along with spermatozoa and bisects the size of the zygote.

"**விந்து குடியிருந்த திருநாட்டை விட்டேன்**

மாறுகின்ற கத்தரிக்கோல் பட்டந்தனில்

விந்துநின்று விளங்குநதி மையத்துள்ளே

விளங்கு சுவாதிட்டான வெளியிலேதான்" -***திருவள்ளுவர் ஞானவெட்டியான்***

The swadhittanam is to be found between the genital and navel region. The swadhittanam is correlated with adrenal gland which secretes testosterone.

சுக்கிலம் குணம்

"**உண்மையான சுக்கில முபாயமா யிருந்ததும்**

வெண்மையாகி நீரிலே விரைந்து நீர தானதும்

தண்மையான காயமே தரித்துருவ மானதும்

தெண்மையான ஞானிகள் தெளிந்துரைக்க வேணுமே"

-சிவவாக்கியர் பாடல் எண்.1236----

Sivavakiyaar in the above verses states that the sperm moves through the vagina in a tricky way and mixes with internal secretions and finally to form a "DEW DROP". This dew drop enhances the growth of ovum.

Modern correlation

Basic concepts of physiology states that the movement of the sperm through the uterus is facilitated by the anti peristaltic contractions of uterine muscles.among 200-300 millions of sperm entering female genital tract only a few thousands sperm reach the spot near ovum. Among these few thousands sperm only one succeeds in fertilizing the ovum.

DIAGNOSIS OF DISEASE BY CHARACTERS OF SEMEN:

1. White and akin to the butter, it is excellent.
2. White and curd, it is very good.
3. White and akin to the milk, it is good.
4. White and akin to the buttermilk, it is fair.
5. Akin to the honey in colour and consistency,it is average.
6. Akin to the ghee in colour and weight, it is poor.
7. Akin to the toddy in colour and thickness it is poor.
8. Akin to the water, it is very bad.

SIDDHA PATHOLOGY

The subtle form of primordial elements

1. Earth
2. Water
3. Fire
4. Air
5. Space

In the above the Air element aggravates the urethral pain during purulent discharge from urethra.

The properties of object having the five elemental components

1. Earth - Bulk
2. Water –Soft, giving pleasure, coolness soaking, viscid, slimy and flowing of semen.
3. Fire -Hot
4. Air - Denselessness
5. Space – Sharp and clear

The properties of taste

The ill effect caused by excessive intake of saltiest food leads to a gradual loss of vitality and vigor. The ill effect caused by excessive intake of pungent food leads to **impotency.**

Based on Five Motor Organs

1. Mouth
2. Legs
3. Hands
4. Excretory Organs
5. Reproductive Organs - Reproductive Organs causes Ejaculation, and ensures pleasure on account of reproduction.

The Ten Channels (Dasa Naadi)

1. Idakalai
2. Pingalai
3. Suzhimunai
4. Siguvai
5. Purudan
6. Kanthari
7. Aththi
8. Alampudai
9. Sangini
10. Gugu.

- Sangini – Located in Genital Organs.
- Gugu – Located in Anorectal region.

The five kinds of Aasayams:

1. Amarvasayam
2. Pakirvasayam
3. Salavasayam
4. Malavasayam
5. Sukkilavasayam – specified activities are semen secretion and storage.

KOSAM (FIVE SHEATHS):

1. Aanamaya kosam
2. Pranamaya kosam
3. Manomaya kosam – constituted by the Mind and the Sense organs
4. Vingnanamaya kosam
5. Anaandhamaya Kosam – constituted by the Prana and Reproductive system

EIGHT PASSIONS:

1. Kaamam
2. Kurotham
3. Lopam
4. Mokam
5. Madham
6. Maacharyam
7. Idumbai
8. Ahankaram

***KAAMAM – Sexual desire**

THE THREE HUMOURS

1. Vatham
2. Pitham
3. Kapham

VATHAM- 10 different types:

1. Pranan
2. Abanan
3. Vyanan
4. Udhyanan

5. Samanan
6. Nagan
7. Koorman
8. Kirukaran
9. Devadhaththan
10. Dhananjayan.

- ABANAN – the downward Air. Responsible for excretion of urine, faeces and semen
- VYANAN – activates the Voluntary and involuntary muscles.
- DEVADATHTHAN – attributes human passions.

PITHAM 5 different types:

1. Analpasaka pitham
2. Vanna eri
3. Aarralankai
4. Ulloli thee
5. Nokkazhal

- AARRALANKAI – improves Blood
- ULLOLI THEE – gives color and brightness to the skin.

KAPHAM – 5 different types:

1. Ali aiyum
2. Neerpi aiyum
3. Suvaikaan aiyam
4. niraivu aiyam
5. Onri ayam

- Seats of kabham- Urinary bladder, Genital organs which makes the urine and Semen come out of the body.

SEVEN PHYSICAL CONSTITUTIONS

1. **Saarum** (Chyle): This gives mental and physical perseverance. .
2. **Senneer** (Blood): Imparts colour to the body, nourishes the body and is responsible for the Ally and intellect of an individual
3. **Oon** (Muscle): It gives shape to the body according to the physical activity and covers bone.

4. **Kozhuppu** (Adipose tissue): it lubricates the joints and other parts of the body to function smoothly
5. **Enbu** (Bone): Supports the frame and responsible for the postures and movements of body.
6. **Moolai** (Bone marrow): It occupies the medulla of the bones and gives strength and softness to the muscles.
7. **Sukkilam** (Sperm): It is responsible for reproduction.
    - Excess Sukilam causes love and lust towards women and urinary calculi.
    - Decreased sukkilam causes failure in reproduction, pain in the genitalia etc.

FOURTEEN NATURAL URGES

Semen is the one of the fourteen urges

"**சுக்கிலந் தனைய டக்கின்**

சுரமுட னீர்க்கட் டாகும்

பக்கமாங் கைகால் சந்து

பாரநோய் வழியி றங்கும்

மிக்கமார் நோயுண் டாகும்

மிகுத்திடும் பிரமே கந்தான்

தக்கதோர் போது மாகின்

தரித்திடும் வாயுக் கூறே"

-சித்த மருத்துவாங்க சுருக்கம்

If Semen is controlled, it leads to fever,,oliguria, joint pain, urinary infection, spermatorrhoea, Leucorrhoea and chest pain.

Significance of sperm implantation period:

Implantation of sperm occurs few days before full moon leads to unhappiness.

- Implantation of sperm occur six days after full moon leads to happiness
- Four mugurthams before dawn is the right time to implantation of sperm
- One mugurtham is equal to one and a half hour

சுக்கில வாதம்

வாதமா முடலுருகி மிகவும் வற்றி

மலமூத்திரஞ் சிக்கியே கீழ்விழாமல்

நாதமாம் நாக்கோடு மூக்குதன்னில்

நாணுக்கமா யுதிரந்த னருவி பாயுஞ்

செயவோடு சுவாசமா யருசி யுண்டாஞ்

சூதமாய்ச் சுக்கிலந்தான் றுன்னி யாகுந்

துரியசுக் கிலவாத சூட்சந் தானே. - ***யூகிமுனி***

Symptoms associated with sukkilam

In the above verses yugi muni states that

1. Emaciation
2. Constipation
3. Oliguria
4. Bleeding from the nose
5. Phlegm accumulation due to increased kapham, breathlessness
6. Loss of taste

All the symptoms are associated with affected sukkilam**.**

DIFFERNTIAL DIAGNOSIS:

பதித வாதம்

காரியாய் மிகவார்த்தை பேசும் போது

கழுத்திலுள நரம்புமிக விசைத்து நோவாம்

வாரியாய் வார்த்தைகள்தான் விக்கிப் பேசி

வார்த்தைகள்தான் பேசு வதிற் றெரிந்தி டாது

நாரியார் போகமது விரும்பி டாது

நலுக்கமாய்த் தாதுவெலா மிளைத்துக் காணும்

பாரியா யடிக்கடிக்குப் பசியே யுண்டாகும்

பதிதமாம் வாதமென்றே பகர லாமே!

-யூகி முனி வாத காவியம்

Due to over talking more pain wil be felt neck aggravated in the cervical plexus. Loss of sexual,general weakness, increase appetite.

வாத உபகதம்

ஆண்மையாங் காலோடு கையுஞ் சந்து
அங்க மெலா மிகத்திமிர்ந்து சாணி தானும்
பூண்மையாப் பூசினது போலே காணும்
புரண்டுதான் விறுவிறுத்துப் புளக மாகிப்
பாண்மையாங் காதசையு முஷ்ணமாகிப்
பசித்துமே மிகநாணி நடை கொடாது
வாண்மையாம் வாட்டமுறு மயக்க மாகும்
வாதவுப கதந்தன்னை வகுத்த வாறே!

-யூகி முனி வாத காவியம்

Numbness of joints of upper and lower limbs,increased body heat,appetite,excessive tiredness and inability to walk, giddiness.

LINE OF TREATMENT

In Siddha system the main aim of the treatment is to cure Udarpini (due to Mukkuttram) and Manapini (due to changes in Mukkunam). Treatment is not only for perfect healing but also for the prevention and rejuvenation.

It is essential to know the disease, the aetiology, the nature of the patient, severity of the illness, the seasons and the time of occurrence must be observed clearly.

Line of treatment is as follows:

1. Neekkam (Treatment)
2. Niraivu (Rejuvenation)
3. Kaapu (Prevention)

Thiruvalluvar describes the duty of the physician, i.e. study the disease, aetiology, seek subsiding ways and do what is proper and effective.

"நோய் நாடி நோய் முதல் நாடி அது தணிக்கும்

வாய் நாடி வாய்ப்பச் செயல்"

"உற்றானளவும் பிணியளவுங் காலமும்

கற்றான் கருதிச் செயல்"

- திருக்குறள்.

1) NEEKKAM (Treatment in Siddha):

The aim of Neekkam is based on to bring the deranged Thodams to normal equilibrium state.

To treat the patient with internal medicine and external medicine

Siddha system of Medicine is based on Mukkutra Theory and hence the treatment is mainly aimed to bring the three thodams to equilibrium state and thereby restoring the physiological condition of the seven Thathus.

The three Thodams organise, regularise and integrate the body structure and their functions. They are always kept in a state of balance by thought, word, deed and food. Any imbalance will lead to disease. The imbalanced thodams are balanced by administrating purgatives or emetics or application of Anjanam (application on eyes) and followed by the appropriate systemic therapy by giving Siddha drugs.

"விரேசனத்தால் வாதந் தாழும்"

"வமனத்தால் பித்தம் தாழும்"

"நசிய அஞ்சனத்தால் கபம் தாழும்" - ***சித்த மருத்துவாங்கச் சுருக்கம்***

Before treating with the trail drug the patients were advised to take oil bath with Arraku Thylam to normalize the vitiated pitham to equilibrium.

The purgatives should be given before starting the trial to normalize the deranged Thodams to normal.

In this study the purgation is induced by giving Agasthiyar kulambu - 130 mg with hot water in early morning in empty stomach.

2) NIRAIVU (Rejuvenation):

The word literally means the power of securing the body from the effect of age.According to Siddhars science rejuvenation does not necessarily mean restoring the old to youth for it may simply mean the maintenance of youth without reaching the old age.

So rejuvenation is a means for prolonging life & forms a part of immortality.

T.V. Sambasivam pillai dict.

(Physical, psychological, social and economic rehabilitation and reassurance of

Individuals are known as Niraivu).

3. KAPPU (PREVENTION):

The prevention methods for Aan Maladu are as follows:

- Advised to take oil bath twice a week.
- Advised to avoid smoking alcohol and using tobacco of any kind.
- Advised to avoid sour rich food suffs.

4) DIETARY RESTRICTIONS:

In siddha system of medicine the importance of dietary habits also emphasiszed for the diseases management and prevention. This line is well understood in these verses,

“உணவே மருந்து மருந்தே உணவு”.

“மருந்தென வேண்டாவாம் யாக்கைக்கு அருந்தியது

அற்றது போற்றி உணின்”. ***- திருக்குறள்***

In diseased condition diet restrictions or paththiyam are strictly followed to increase the effectiveness of medicine, and to reducing the severity of diseases. This is given in the following verse,

“பத்தியத்தினாலே பலன் உண்டாகும் மருந்து

பத்தியங்கள் போனால் பலன்போகும் - பத்தியத்தில்

பத்தியமே வெற்றிதரும் பண்டிதர்க்கு ஆதலினால்

பத்தியமே உத்தியென்று பார்” *- தேரையர் வெண்பா.*

இச்சா பத்தியத்தில் நீக்கும் பொருட்கள்:

"கடுகு நற்றிலத் தெண்ணைய் கூழ்பாண்டங்கள் கடலை

வருவதாகிய தெங்குமா வருக்கை நற்காயம்

மடிவிலாத வெள்ளுள்ளிகொள் புகையிலை மதுபெண்

இடறு பாகலோ டகத்தி நீக்கிடலிச்சா பத்தியம்"

- சித்த மருத்துவாங்கச் சுருக்கம்

கடுகு, எள்நெய், கல்யாணபூசணிக்காய், கள், கடலை, தேங்காய், மாங்காய், பலா, காயம், உள்ளிப்பூண்டு, கொள், புகையிலை, பெண்கள் சேர்க்கை, பாகல், அகத்தி இவைகளை இச்சா பத்தியத்தில் நீக்க வேண்டும்.

"புளிதுவர் விஞ்சும் கறியால் பூரிக்கும் வாதம்"

- நோய் நாடல் நோய் முதல் நாடல் திரட்டு

“தாளி முருங்கைத் தழை தூதுளம் பசலை

வாளிலறு கீரையுநெய் வார்த்துண்ணி- லாளியென

விஞ்சுவார் போகத்தில் வீம்புரைத்த பெண்களெலாங்

கெஞ்சுவார் பின்வாங்கிக் கேள்”

-குணபாடம் மூலிகை வகுப்பு

நறுந்தாளி, **நன்முருங்கை**, **தூதுணம்**, **பசலை**, **அறுகீரை இவற்றுள் யாதேனும் ஒன்றை புளி நீக்கிச் சமைத்து நெய் சேர்த்துக் காலையில் மாத்திரம் நாற்பது நாள் உண்ண**, **ஆண்மைப் பெருகும்**.

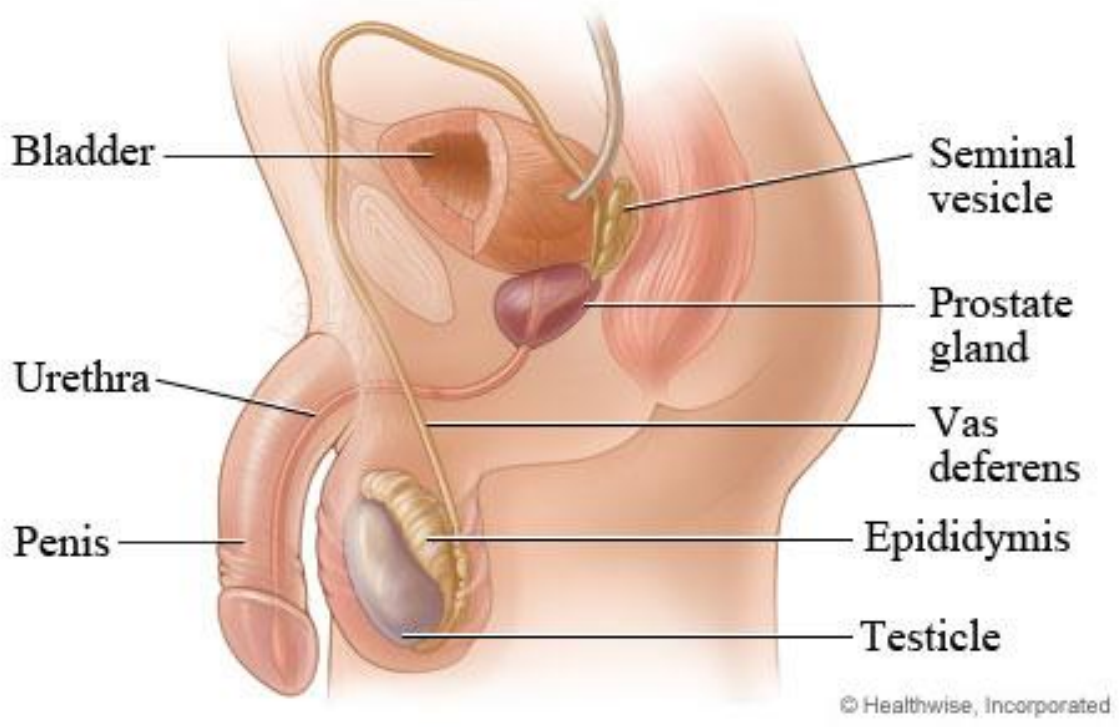
தவிர்க்க வேண்டியவை:

- **பகற்பொழுதில் புணர்ச்சியில் ஈடுபடக் கூடாது**
- **வயதில் மூத்த மாதரைப் புணரக் கூடாது**
- **பெண்களிடத்தில் மாதத்திற்கு ஒருமுறை மட்டும் புணர்ச்சியில் ஈடுபட வேண்டும்**
- 4 **நாட்களுக்கு எண்ணெய் முழுக்கு செய்ய வேண்டும்**

-சித்த மருத்துவாங்க சுருக்கம்

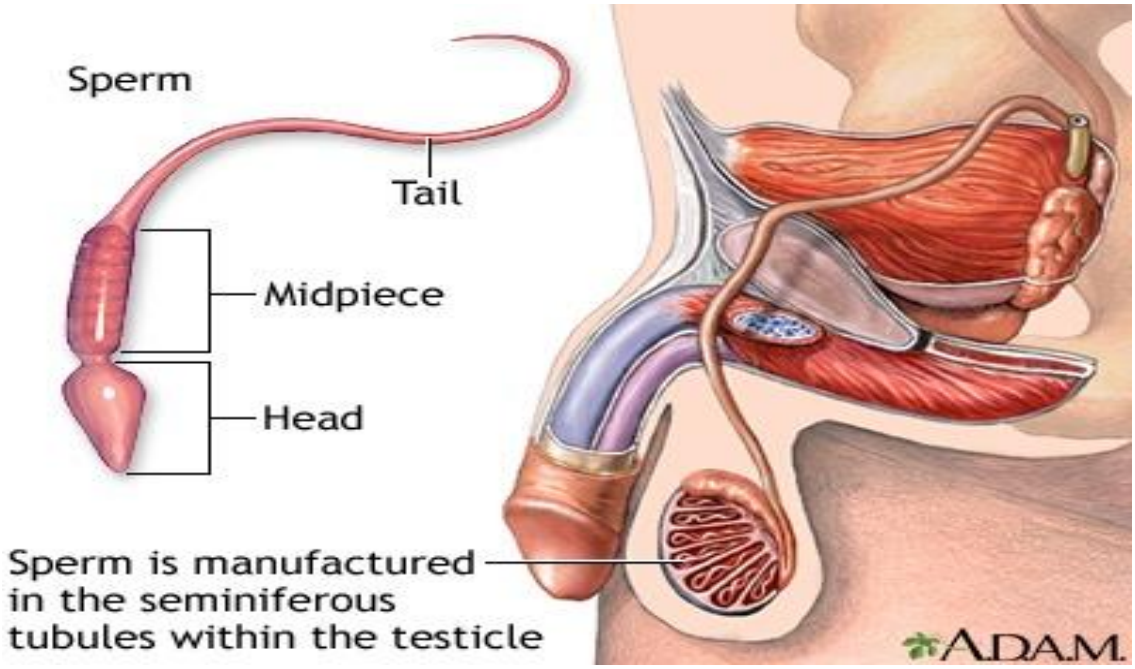
THE MALE REPRODUCTIVE SYSTEM

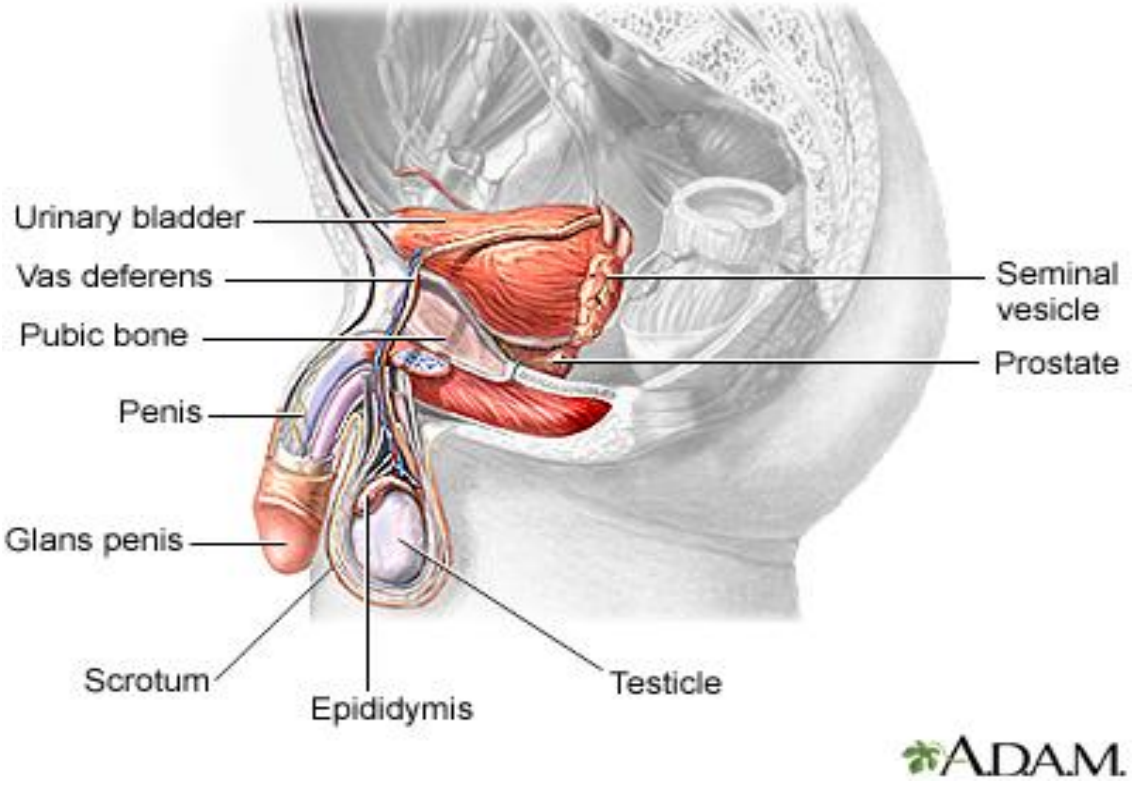
Male Reproductive System



The purpose of the organs of the male reproductive system is to perform the following functions:

- To produce, maintain, and transport sperm (the male reproductive cells) and protective fluid (semen)
- To discharge sperm within the female reproductive tract during sex
- To produce and secrete male sex hormones responsible for maintaining the male reproductive system


Sperm
Tail
Midpiece
Head
Sperm is manufactured in the seminiferous tubules within the testicle
A.D.A.M.


Urinary bladder
Vas deferens
Pubic bone
Penis
Glans penis
Scrotum
Epididymis
Testicle
Seminal vesicle
Prostate
A.D.A.M.

Unlike the female reproductive system, most of the male reproductive system is located outside of the body. These external structures include the penis, scrotum, and testicles.

- **Penis**: This is the male organ used in sexual intercourse. It has three parts: the root, which attaches to the wall of the abdomen; the body, or shaft; and the glans, which is the cone-shaped part at the end of the penis. The glans, also called the head of the penis, is covered with a loose layer of skin called foreskin. This skin is sometimes removed in a procedure called circumcision. The opening of the urethra, the tube that transports semen and urine, is at the tip of the penis. The penis also contains a number of sensitive nerve endings.

The body of the penis is cylindrical in shape and consists of three circular shaped chambers. These chambers are made up of special, sponge-like tissue. This tissue contains thousands of large spaces that fill with blood when the man is sexually aroused. As the penis fills with blood, it becomes rigid and erect, which allows for penetration during sexual intercourse. The skin of the penis is loose and elastic to accommodate changes in penis size during an erection.

- The internal organs of the male reproductive system, are called as accessory organs which includes the following:

- **Epididymis:** The epididymis is a long, coiled tube that rests on the backside of each testicle. It transports and stores sperm cells that are produced in the testes. It is the job of the epididymis to bring the sperm in to maturity, since the sperms that emerge from the testes are immature and incapable of fertilization. During sexual arousal, contractions force the sperm into the vas deferens.

- **Vas deferens**: The vas deferens is a long, muscular tube that travels from the epididymis into the pelvic cavity, to just behind the bladder. The vas deferens transports mature sperm to the urethra, the tube that carries urine or sperm to outside of the body, in preparation for ejaculation.

- **Ejaculatory ducts**: These are formed by the fusion of the vas deferens and the seminal vesicles (see below). The ejaculatory ducts empty into the urethra.

- **Urethra:** The urethra is the tube that carries urine from the bladder to outside of the body. In males, it has the additional function of ejaculating semen when the man reaches orgasm. When the penis is erect during sex, the flow of urine is blocked from the urethra, allowing only semen to be ejaculated at orgasm.

- **Seminal vesicles:** The seminal vesicles are sac-like pouches that attach to the vas deferens near the base of the bladder. The seminal vesicles produce a sugar-rich fluid (fructose) that provides sperm with a source of energy to help them move. The fluid of the seminal vesicles makes up most of the volume of a man's ejaculatory fluid, or ejaculate.

- **Prostate gland**: The prostate gland is a walnut-sized structure that is located below the urinary bladder in front of the rectum. The prostate gland contributes additional fluid to the ejaculate. Prostate fluids also help to nourish the sperm. The urethra, which carries the ejaculate to be expelled during orgasm, runs through the center of the prostate gland.

- **Bulbourethral glands**: Also called Cowper's glands, these are pea-sized structures located on the sides of the urethra just below the prostate gland. These glands produce a clear, slippery fluid that empties directly into the urethra. This fluid serves to lubricate the urethra and to neutralize any acidity that may be present due to residual drops of urine in the urethra.

Function of the Male Reproductive System

The entire male reproductive system is dependent on hormones, which are chemicals that regulate the activity of many different types of cells or organs. The primary hormones involved in the male reproductive system are follicle-stimulating hormone, luteinizing hormone, and testosterone.

Follicle-stimulating hormone is necessary for sperm production (spermatogenesis), and luteinizing hormone stimulates the production of testosterone, which is also needed to make sperm. Testosterone is responsible for the development of male characteristics, including muscle mass and strength, fat distribution, bone mass, facial hair growth, voice change, and sex drive.

Semen, which contains sperm (reproductive cells), is expelled (ejaculated) through the end of the penis when the man reaches sexual climax (orgasm). When the penis is erect, the flow of urine is blocked from the urethra, allowing only semen to be ejaculated at orgasm.

- **Scrotum:** This is the loose pouch-like sac of skin that hangs behind and below the penis. It contains the testicles (also called testes), as well as many nerves and blood vessels. The scrotum acts as a "climate control system" for the testes. For normal sperm development, the testes must be at a temperature slightly cooler than body temperature. Special muscles in the wall of the scrotum allow it to contract and relax, moving the testicles closer to the body for warmth or farther away from the body to cool the temperature.

- **Testicles (testes):** These are oval organs about the size of large olives that lie in the scrotum, secured at either end by a structure called the spermatic cord. Most men have two testes. The testes are responsible for making testosterone, the primary male sex hormone, and for generating sperm. Within the testes are coiled masses of tubes called seminiferous tubules. These tubes are responsible for producing sperm cells.

Sperm

- Sperm are made in hundreds of microscopic tubes, known as seminiferous tubules, which make up most of the testicles.

Surrounding these tubules are clumps of tissue containing Leydig cells, which produce testosterone when stimulated by luteinizing hormone (LH).

- Sperm Development. The life cycle of sperm takes about 74 days:

- Sperm in the begining partially embedded in nurturing Sertoli cells, which are located in the lower parts of the seminiferous tubules.

- As they mature move along,and are stored in the upper part of the seminiferous tubules. Young sperm cells are known as spermatids.

- When the sperm has completed the development of its head and tail, it is released from the cell into the epididymis. This C-shaped tube is 1/300 of an inch in diameter and about 20 feet long. It loops back and forth on itself within a space that is only about one and a half inches long. The sperm's journey through the epididymis takes about 3 weeks.

The fluid in which the sperm is transported contains sugar in the form of fructose, which provides energy as the sperm matures. In the early stages of its passage, the sperm cannot swim in a forward direction and can only vibrate its tail weakly. By the time the sperm reaches the end of the epididymis, however, it mature and looks like a microscopic squirming tadpole.

At maturity, each healthy sperm consists of a head that contains the man's genetic material (his DNA) and a tail that lashes back and forth at great speed to propel the head forward at about four times its own length every second. The ability of a sperm to move forward rapidly and straight is probably the most significant determinant of male fertility.

Ejaculation. When a man experiences sexual excitement, nerves stimulate the muscles in the epididymis to contract, which forces the sperm out through the penis:

After being produced in the testicle, the sperm first pass through the epididymis and then into one of two rigid and wire-like muscular channels, called the vasa deferentia. (A single member of this pair of channels is called a vas deferens.)

Muscle contractions in the vas deferens from sexual activity propel the sperm along past the seminal vesicles. These are clusters of tissue that contribute fluid, called seminal fluid, to the sperm. The vas deferens also collects fluid from the nearby prostate gland. This mixture of various fluids and sperm is the semen.

Each vas deferens then joins together to form the ejaculatory duct. This duct, which now contains the sperm-containing semen, passes down through the urethra. (The urethra is the same channel in the penis through which a man urinates, but during orgasm, muscles close off the bladder so that urine cannot enter the urethra.)

The semen is forced through the urethra during ejaculation, the final stage of orgasm when the sperm is literally shot out of the penis.

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Sperm Abnormalities

Sperm abnormalities can be caused by a range of factors, including congenital birth defects, disease, chemical exposure, and lifestyle habits. In many cases,the causes of sperm abnormalities are unknown.

Sperm abnormalities are categorized by whether they affect sperm count, sperm movement, or sperm shape. They include:

- **Low Sperm Count (Oligospermia**). sperm count of less than 20 million/mL is considered as Azoospermia refers to the complete absence of sperm cells in the ejaculate. Partial obstruction anywhere in the long passages through which sperm pass can reduce sperm counts. Sperm count varies widely over time, and temporary low counts are common. A single test that reports a low count may not be a representative result.

- **Poor Sperm Motility (Asthenospermia).** Sperm motility is the sperm's ability to move. If movement is slow or not in a straight line, the sperm have difficulty invading the cervical mucus or penetrating the hard outer shell of the egg. If 60% or more of sperm have normal motility, the sperm is said to be average in quality. If less than 40% of sperm are able to move in a straight line, the condition is considered abnormal. Sperm that move sluggishly may have genetic or other defects that render them incapable of fertilizing the egg. Poor sperm motility may be associated with DNA fragmentation and may increase the risk for passing on genetic diseases.

- **Abnormal Sperm Morphology (Teratospermia**). Morphology refers to shape and structure. Abnormally shaped sperm cannot fertilize an egg. About 60% of the sperm should be normal in size and shape for adequate fertility. The perfect sperm structure is an oval head and long tail.

In addition to providing the fluid that transports the sperm, semen also has other benefits:

- It provides a very short-lived alkaline environment to protect sperm from the harsh acidity of the female vagina. (If the sperm do not reach the woman's cervix within several hours, the semen itself becomes toxic to sperm and they die.)

- It contains a gelatin-like substance that prevents it from draining from the vagina too quickly.

- It contains sugar in the form of fructose to provide instant energy for sperm locomotion.

- The sperm's passage to the egg is a difficult journey.Semen provides the pathway for the sperm to reach the egg.

- Usually about 100 - 300 million sperm are delivered into the ejaculate at any given time. Even under normal conditions only about 15% of these millions of sperm are strong enough to fertilize an egg.

- After the stress of ejaculation, only about 400 sperm survive the orgasm to continue the journey.

- Out of this number, only about 40 sperm survive the challenges posed by the semen and the environment of the vagina to reach the vicinity of the egg. Normally, the cervical mucus forms an impenetrable barrier to sperm. However, when a woman ovulates (releases her egg, the oocyte), the mucous lining thins to allow sperm penetration.

- Sperm that manage to reach the mucus lining in the woman's cervix (the lower part of her uterus) must survive about four more days to reach the woman's fallopian tubes. (Here, the egg is positioned for fertilization for only 12 hours each month.)

- The few remaining sperm that penetrate the cervical mucus and are able to reach the fallopian tubes become capacitated.

- Capacitation is a one-time explosion of energy that completes the sperm's journey. It boosts the motion of the sperm and triggers the actions of the acrosome, a membrane that covers the head of the sperm and resembles a warhead. The acrosome is dissolved, and enzymes contained within it are released to allow the sperm to drill a hole through the tough outer coating of the egg.

- In the end, only one sperm gets through to fertilize the egg

Testosterone

A testosterone test checks the level of this male hormone (androgen) in the blood.Testosterone affects sexual features and development. In men, it is made in large amounts by the testicles. In both men and women, testosterone is made in small amounts by the adrenal glands; and, in women, by the ovaries.

The pituitary gland controls the level of testosterone in the body. When the testosterone level is low, the pituitary gland releases a hormone called luteinizing hormone (LH). This hormone tells the testicles to make more testosterone. See a picture of the pituitary gland .

Before puberty, the testosterone level in boys is normally low. Testosterone increases during puberty. This causes boys to develop a deeper voice, get bigger muscles, make sperm, and get facial and body hair. The level of testosterone is the highest around age 40, then gradually becomes less in older men.

In women, the ovaries account for half of the testosterone in the body. Women have a much smaller amount of testosterone in their bodies compared to men. But testosterone plays an important role throughout the body in both men and women. It affects the brain, bone and muscle mass, fat distribution, the vascular system, energy levels, genital tissues, and sexual functioning.

Most of the testosterone in the blood is bound to a protein called sex hormone binding globulin (SHBG). Testosterone that is not bound ("free") can also be checked if a man or a woman is having sexual problems.

Significance of testosterone:

- A low amount of testosterone can lead to low sperm counts.
- . A low level of testosterone may lower a man's sex drive or not allow him to have an erection (erectile dysfunction).
- See whether a high level of testosterone is causing a boy younger than age 10 to have early signs of puberty.
- Check a decreased sex drive in a woman. This may be due to the level of testosterone in her body.
- Find out why a woman is developing male features, such as excessive facial and body hair (hirsutism) and a deep voice.
- Find out why a woman is having irregular menstrual periods.
- See if testosterone-lowering medicines are working in a man with advancedprostate cancer.
- Find the cause of osteoporosis in a man.

A testosterone test checks the level of androgen(male sex hormone) in the blood.

Normal

The normal values listed here-called a reference range-are just a guide. These ranges vary from lab to lab, and your lab may have a different range for what's normal.

Table : 1

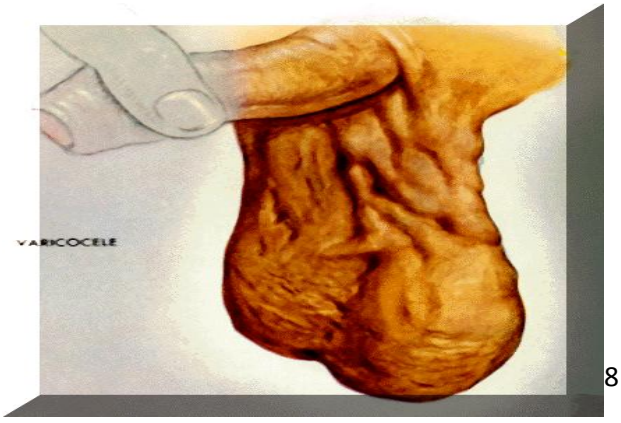
Total testosterone	
Men	270-1070 ng/dL (9-38 nmol/L)
Women	15-70 ng/dL (0.52-2.4 nmol/L)
Children	2-20 ng/dL or 0.07-0.7 nmol/L

The testosterone level for a postmenopausal woman is about half the normal level for a healthy, nonpregnant woman. And a pregnant woman will have 3 to 4 times the amount of testosterone compared to a healthy, nonpregnant woman.

Table : 2

Free testosterone	
Men	50-210 pg/mL (174-729 pmol/L)
Women	1.0-8.5 pg/mL (3.5-29.5 pmol/L)

The etiologic factors in male infertility continue to be debated and there is incomplete knowledge about its pathophysiology.



A varicocele develops when the one way valves in these spermatic veins are damaged causing an abnormal back flow of blood from the abdomen into the scrotum creating a hostile environment for sperm development. Varicocoeles may cause reduced sperm count and abnormal sperm morphology which cause infertility. Variococles can usually be diagnosed by a physical examination of the scrotum which can be aided by the Doppler stethoscope and scrotal ultrasound. Varicocoele can be treated in many ways but the most successful treatments involve corrective surgery.

INVESTIGATION

1.Semen sample

A semen sample is collected by masturbation. Patient is adviced to urinate and then wash and rinse their hands and penis before collecting the semen in a sterile cup. Lubricants or condoms should not be used when collecting the sample. While collect the semen sample at home, be sure to get it to the lab or clinic within 1 hour. Keep the sample at body temperature and out of direct sunlight. The sample cannot be collected by having sexual intercourse and then withdrawing when you ejaculate because vaginal fluid may be mixed with the sperm.

2.Collection of Semen

Patient was asked to avoid any sexual activity that results in ejaculation for 2 to 5 days before a semen analysis. This helps to ensure that sperm count will be at its highest, and it improves the reliability of the test. If possible, do not avoid sexual activity for more than 1 to 2 weeks before this test, because a long period of sexual inactivity can result in less active sperm.

Patient was asked to avoid drinking alcohol for a few days before the test.

- The most common way to collect semen is by masturbation, directing the semen into a clean sample cup. Do not use a lubricant.

- Patient was advised to collect a semen sample during sex by withdrawing their penis from their partner just before ejaculating (coitus interruptus). patient then ejaculate into a clean sample cup. This method can be used after a vasectomy to test for the presence of sperm, but other methods will likely be recommended if you are testing for infertility.

Sperm collection by surgical method:

If sperm cannot be collected by means of masturbation, they are surgically removed from a testicle through a small incision. This method of sperm retrieval is done when there is a blockage that prevents sperm from being ejaculated or when there is a problem with sperm development. To screen for possible genetic problems that could affect offspring, experts recommend that men with little or no sperm in their semen (not due to a blockage) have genetic testing before they proceed with ICSI.

3. Sperm Penetration Tests

Sperm penetration tests were check carried out to whether a man's sperm can move through cervical mucus and the fallopian tubes to join with (fertilize) an egg. This test is usually done when a couple is having trouble becoming pregnant (infertility).

SEMEN ANALYSIS

- Volume. This is a measure of how much semen is present in one ejaculation.
- Liquefaction time. Semen is a thick gel at the time of ejaculation and normally becomes liquid within 20 minutes after ejaculation. Liquefaction time is a measure of the time taken by the semen to liquefy.
- Sperm count. This is a count of the number of sperm present per milliliter (mL)of semen in one ejaculation.
- Sperm morphology. This is a measure of the percentage of sperm that have a normal shape.
- Sperm motility. This is a measure of the percentage of sperm that can move forward normally. The number of sperm that show normal forward movement in a certain amount of semen can also be measured (motile density).
- pH. This is a measure of the acidity (low pH) or alkalinity (high pH) of the semen.
- White blood cell count. White blood cells are not normally present in semen.
- Fructose level. This is a measure of the amount of a sugar called fructose in the semen. The fructose provides energy for the sperm

Significance of Semen Analysis:

A semen analysis is done to determine whether:

- A man has a reproductive problem that is causing infertility.
- A vasectomy has been successful.
- The reversal of a vasectomy has been successful.

Intracytoplasmic Sperm Injection for Infertility

Intracytoplasmic sperm injection (ICSI) is an assisted reproductive technology (ART) used to treat sperm-related infertility problems. ICSI is used to enhance the fertilization phase of in vitro fertilization (IVF) by injecting a single sperm into a mature egg. The fertilized egg is then placed in a woman's uterus or fallopian tube.

4.Antisperm Antibody Test

An antisperm antibody test looks for special proteins (antibodies) that fight against a man's sperm in blood, vaginal fluids, or semen. The test uses a sample of sperm and adds a substance that binds only to affected sperm.

Semen can cause an immune system response in either the man's or woman's body. The antibodies can damage or kill sperm. If a high number of sperm antibodies come into contact with a man's sperm, it may be hard for the sperm to fertilize an egg. The couple has a hard time becoming pregnant. This is called immunologic infertility.

A man can make sperm antibodies when his sperm come into contact with his immune system. This can happen when the testicles are injured or after surgeries (such as a biopsy or vasectomy) or after a prostate gland infection. The testicles normally keep the sperm away from the rest of the body and the immune system.

A woman can have an allergic reaction to her partner's semen and make sperm antibodies. This kind of immune response is not fully understood but may affect fertility. This is a rare cause of infertility.

Significance of Antisperm antibody test

The antisperm antibody test may be done if:

- A cause for infertility cannot be found. Experts disagree about the usefulness of the test because the result may not change the treatment.
- The results from another fertility test, such as the postcoital test, are not clear.
- An antisperm antibody test looks for special proteins (antibodies) that fight against a man's sperm in blood, vaginal fluids, or semen. The higher the level of antibody-affected sperm found in the semen, the lower the chance of the sperm fertilizing an egg.

Medical causes for Male infertility

Problems with male fertility can be caused by a number of health issues and medical treatments. More than 90% of male infertility cases are due to low sperm counts, poor sperm quality, or both. The remaining cases of male infertility can be caused by a number of factors including anatomical problems, hormonal imbalances, and genetic defects

Varicocele: A varicocele is a swelling of the veins that drain the testicle. It's a common cause of male infertility. This may prevent normal cooling of the testicle, leading to reduced sperm count and fewer moving sperm.

Infection: Some infections can interfere with sperm production or sperm health, or can cause scarring that blocks the passage of sperm. These include some sexually transmitted infections, including chlamydia and gonorrhea; inflammation of the prostate (prostatitis); and inflamed testicles due to mumps (mumps orchitis).

Ejaculation issues: Retrograde ejaculation occurs when semen enters the bladder during orgasm instead of emerging out the tip of the penis. Various health conditions can cause retrograde ejaculation, including diabetes, spinal injuries, medications, and surgery of the bladder, prostate or urethra. Some men with spinal cord injuries or certain diseases can't ejaculate semen, even though they still produce sperm.

Antibodies that attack sperm: Anti-sperm antibodies are immune system cells that mistakenly identify sperm as harmful invaders and attempt to eliminate them.

Tumors: Cancers and nonmalignant tumors can affect the male reproductive organs directly or can affect the glands that release hormones related to reproduction, such as the pituitary gland. In some cases, surgery, radiation or chemotherapy to treat tumors can affect male fertility.

Undescended testicles: In some males, during fetal development one or both testicles fail to descend from the abdomen into the sac that normally contains the testicles (scrotum). Decreased fertility is more likely in men who have had this condition.

Hormone imbalances: Infertility can result from disorders of the testicles themselves or an abnormality affecting other hormonal systems including the hypothalamus, pituitary, thyroid and adrenal glands. Low testosterone (male hypogonadism) and other hormonal problems have a number of possible underlying causes.

Sperm duct defects: The tubes that carry sperm (sperm ducts) can be damaged by illness or injury. Some men experience blockage in the part of the testicle that stores sperm (epididymis) or a blockage of one or both of the tubes that carry sperm out of the testicles. Men with cystic fibrosis and some other inherited conditions may be born without sperm ducts altogether.

Chromosome defects: Inherited disorders such as Klinefelter's syndrome — in which a male is born with two X chromosomes and one Y chromosome (instead of one X and one Y) — cause abnormal development of the male reproductive organs. Other genetic syndromes associated with infertility include cystic fibrosis, Kallmann's syndrome, Young's syndrome and Kartagener syndrome.

Problems with sexual intercourse: These can include trouble keeping or maintaining an erection sufficient for sex (erectile dysfunction), premature ejaculation, painful intercourse, anatomical abnormalities such as having a urethral opening beneath the penis (hypospadias), or psychological or relationship problems that interfere with sex.

Celiac disease: A digestive disorder caused by sensitivity to gluten, celiac disease can cause male infertility. Fertility may improve after adopting a gluten-free diet.

Certain medications: Testosterone replacement therapy, long-term anabolic steroid use, cancer medications (chemotherapy), certain antifungal medications, some ulcer drugs and certain other medications can impair sperm production and decrease male fertility.

Environmental causes

Over exposure to certain environmental elements such as heat, toxins and chemicals can reduce sperm production or sperm function. Specific causes include:

- **Industrial chemicals**: Extended exposure to benzenes, toluene, xylene, pesticides, herbicides, organic solvents, painting materials and lead may contribute to low sperm counts.

- **Heavy metal exposure:** Exposure to lead or other heavy metals also may cause infertility.

- **Radiation or X-rays:** Exposure to radiation can reduce sperm production, though it will often eventually return to normal. With high doses of radiation, sperm production can be permanently reduced.

- **Exposure to heat:** Frequent use of saunas or hot tubs may temporarily lower your sperm count. Sitting for long periods, wearing tight clothing or working on a laptop computer for long stretches of time also may increase the temperature in your scrotum and slightly reduce sperm production. The type of underwear you wear is unlikely to make a significant difference in male fertility

HEALTH, LIFESTYLE AND OTHER CAUSES

Some other causes of male infertility include:

- **Illegal drug use:** Anabolic steroids taken to stimulate muscle strength and growth can cause the testicles to shrink and sperm production to decrease. Use of cocaine or marijuana may temporarily reduce the number and quality of your sperm as well.

- **Alcohol use**: Drinking alcohol can lower testosterone levels, cause erectile dysfunction and decrease sperm production. Liver disease caused by excessive drinking also may lead to fertility problems.

- **Occupation:** Certain occupations can increase your risk of infertility, including those associated with extended use of computers or video display monitors, shift work, and work-related stress.

- **Tobacco smoking**: Men who smoke may have a lower sperm count than do those who don't smoke. Secondhand smoke also may affect male fertility.

- **Emotional stress:** Stress can interfere with certain hormones needed to produce sperm. Severe or prolonged emotional stress, including problems with fertility, can affect your sperm count.

- **Weight:** Obesity can cause hormone changes that reduce male fertility.

Prolonged bicycling: Prolonged bicycling is another possible cause of reduced fertility due to overheating the testicles. In some cases, bicycle seat pressure on the area behind the testicles (perineum) can cause numbness in the penis and erectile hormonal deficiencies.

Hypogonadism is the general name for a severe deficiency in gonadotropin-releasing hormone (GnRH), the primary hormone that signals the process leading to the release of testosterone and other important reproductive hormones. Low levels of testosterone from any cause may result in defective sperm production.

PSYCHOLOGICAL/PHYSICAL/BEHAVIORAL PROBLEMS

Several sexual problems both psychological and physical in nature. it is difficult to separate the physiological and physical components exist that can affect male fertility.

Erectiledysfunction(ED):

ED is the result of a single, or more commonly a combination of multiple factors. In the past, ED was thought to be the result of psychological problems, but new research indicates that 90 percent of cases are organic in nature. However, most men who suffer from ED have a secondary psychological problem that can worsen the situation like performance anxiety, guilt, and low self-esteem.

common causes of impotence include: diabetes, high blood pressure, heart and vascular disease, stress, hormone problems, pelvic surgery, trauma, venous leak.

Premature Ejaculation:

Is defined as an inability to control the ejaculatory response for at least thirty seconds following penetration. Premature ejaculation becomes a fertility problem when ejaculation occurs before a man is able to fully insert his penis into his partner's vagina. Premature ejaculation can be overcome by artificial insemination or by using a behavioral modification technique called the "squeeze technique" which desensitizes the penis.

Ejaculatory Incompetence:

This rare psychological condition prevents men from ejaculating during sexual intercourse even though they can ejaculate normally through masturbation. This condition sometimes responds well to behavioral therapy; if this technique does not work, artificial insemination can be employed using an ejaculate from masturbation.

RISK FACTORS REGARDING MALE INFERTILITY

A number of risk factors are linked to male infertility. They include:

- Smoking tobacco
- Using alcohol
- Using certain illegal drugs
- Being overweight
- Having certain past or present infections
- Being exposed to toxins
- Overheating the testicles
- Having a prior vasectomy or vasectomy reversal
- Being born with a fertility disorder or having a blood relative with a fertility disorder
- Having certain medical conditions, including tumors and chronic illnesses
- Taking certain medications or undergoing medical treatments, such surgery or radiation used for treating cancer
- Performing certain prolonged activities such as bicycling or horseback riding, especially on a hard seat or poorly adjusted bicycle

Complications of Male infertility

Infertility can be stressful for both you and your partner. Complications can include:

- Surgery or other procedures to treat an underlying cause of low sperm count or other reproductive problems
- Expensive and involved reproductive techniques such as in vitro fertilization
- Stress and relationship difficulties related to the inability to have a child

LIFESTYLE CHANGES

Timing and Monitoring Sexual Activity for Best Results

Both male and female hormone levels fluctuate according to the time of day, and they also vary from day to day and month to month. Some timing tips might be helpful.

Fertility and Seasonal Changes. Some studies have reported higher sperm counts in the winter than in the summer. For women, fertility rates as measured by treatment success are highest in months when days are longest.

Monitoring Basal Body Temperature. To determine the most likely time of ovulation and therefore the time of fertility, a woman should take her body temperature, called her basal body temperature. This is the body's temperature as it rises and falls in accord with hormonal fluctuations.

By studying the temperature patterns after a few months, couples can begin to anticipate ovulation and plan their sexual activity accordingly.

Frequency of Intercourse. It is not clear how often a couple should have intercourse in order to conceive. Some doctors think that having sex more than 2 days a week adds no benefits. In addition, frequent sexual activity lowers sperm count per ejaculation. Some studies have indicated, however, that having intercourse every day, or even several times a day, before and during ovulation, improves pregnancy rates. Although sperm count per ejaculation is low, a constantly replenished semen supply is more likely to result in a fertilized egg.

Dietary Considerations: Everyone should eat a healthy diet rich in fresh fruits, vegetables, and whole grains. Replace animal fats with monounsaturated oils, such as olive oil. Certain specific nutrients and vitamins have been studied for their effects on male infertility and sperm health. They include antioxidant vitamins (vitamin C, vitamin E) and the dietary supplements L-carnitine and L-acetylcarnitine. To date, there is no conclusive evidence that they are effective.

NUTRITIONAL CONSIDERATIONS

Vitamin c and other Anti- oxidants

Free radical or oxidative damage to sperm is thought to be responsible for many cases of idiopathic oligospermia, with high levels of free radicals found in the semen of 40% infertile men. Three factors combine to render sperm particularly susceptible to free radical damage.

A high membrane concentration of polysaturated fatty acids

Active generation of free radicals

A lack of defensive enzymes.

The health of the sperm critically dependent upon antioxidants. Although most free radicals are produced during normal metabolic processes, the environment contributes greatly to the free radical load. Men exposed to increased levels of source of free radicals are much more likely to have abnormal sperm and sperm counts.

Sperm extremely sensitive to free radicals because they are so dependent upon the integrity and fluidity of their cell membrane for proper function. Without proper membrane fluidity, enzymes are activated, which can lead to impaired motility, abnormal structure loss of viability and ultimately death of sperm. The major determinant of membrane fluidity is the concentration of polyunsaturated fatty acids, particularly omega-3 fatty acids which are very susceptible to free radical damage. The sperm have a relative lack of super oxide dismutase and catalase which can prevent oxidative damage.

A common source of oxide is cigarette smoking, which is associated with decreased sperm counts and sperm motility as well as increased frequency of abnormal sperm. Increase in environmental pollution, is thought to be a major contributor to the decreased in sperm counts seen in many industrialized nations. Anti oxidants such as vitamin C, beta carotene, selenium and vitamin E have been shown to be very important in protecting sperm against damage. Vitamin C plays an vital role in protecting the sperm's genetic material (DNA) from damage. Ascorbic acid levels are much higher in seminal fluid compared with other body fluids. When when dietary vitamin C was reduced from 250 to 5mg/ day in healty human subjects, the seminal fluid ascorbic acid decreased by 50% and the number of sperm with damage of DNA increased by 91%.

It is well documented that cigarette smoking greatly reduces vitamin C levels throughout the body. Vitamin E has been shown to play an essential role in inhibiting free radical damage to the unsaturated fatty acids of the sperm membrane. Vitamin E enhances the ability of sperm to fertilize an egg in test tubes.

Fats and oils

Saturated fats, hydrogenated oils, trans-fatty acids, cotton seed, coconut and palm oil should be avoided. Coconut and palm oils are primarily saturated fat, while cotton seed may contain toxic residues, due to heavy spraying of cotton and its high levels of gossypol, a substance known to inhibit the sperm function. Infact, gossypol is being investigated as the " male birth control pill". Its use as an antifertility agent began after studies demonstrated that men who had used crude cotton seed oil as their cooking oil were shown to have low sperm counts followed by total testicular failure. Excessive consumption of saturated fats combined with

inadequate intake of essential fatty acids changes the fatty acid composition of sperm membranes, thus decreasing fluidity and interfering with sperm motility.

The patient must be informed to read food labels carefully and avoid all sources of cotton seed oil and other damaging oils. While the in take of saturated and hydrogenated fats must be eliminated , the intake of polyunsaturated oils should be increased. These oils function in all aspects of sexual function including sperm formation and activity much lower in infertile men with low sperm counts, including that a low zinc status may be the contributing factor to the infertility. Zinc is found in whole grains, legumes, nuts and seeds.

Vitamin B12

Vitamin B12 is involved in cellular replication. A deficiency of vitamin B12 leads to reduced sperm counts and sperm motility.

Arginine

The amino acids arginine is required for the replication of cells, making it essential in sperm formation.

Carnitine

Carnitine is essential in the transport of fatty acids in to the mitochondria. A deficiency of carnitine results in a decrease in fatty acid concentrations in the mitochondria and reduced energy production. Carnitine concentrations are extremely high in the epididymis and sperm , suggesting a role for carnitine in male reproductive function. The epididymis derives the majority of its energy requirements from fatty acids, as do the sperm, during transport through the epididymis . after the ejaculation, the motility of sperm correlates directly with carnitine content.

The higher the carnitine content , the more motile are the sperm. Supplementing the diet with L- carnitine may be useful in restoring male fertility.

MATERIAL AND METHODS

STANDARD OPERATING PROCEDURE OF THE TRIAL DRUG

POONAIKALI VITHAI CHOORANAM

SOURCE OF RAW DRUGS:

The required raw drugs for the preparation of Poonaikali Vithai chooranam will be purchased from a well reputed country shop. The raw drugs will be authenticated by the Asst.Prof of medicinal botany at NIS. Then the raw drugs will be purified as mentioned in siddha literature. The medicine is prepared in Gunapadam lab of National Institute of Siddha.

REQUIRED RAW DRUGS:

1. Poonaikali vithai(Mucuna *pruriens,* Linn Dc)
2. Siru nerunjil vithai (Tribulus *terrestris,*Linn)
3. Thanneer vittan kizhangu (Asparagus *racemosus,*Wild)
4. Mullilavu ver (Bombax *malabaricum,*Dc)
5. Nelli ver (Phyllanthus *emblica,*Linn)
6. Seenthil sarkarai (Tinospora *cordifolia,*Wild) and
7. Karkandu podi (Quantity equal to the powder of all the above)

METHOD OF PURIFICATION :

(Ref :Sigicha Rathina Deepam, Author :C.Kannusamipillai. Edition 2007)

POONAIKALI VITHAI CHOORANAM (Internal)

1. Poonaikali vithai(Mucuna *pruiens,* Linn Dc)
    a. Part used :Seed
    b. Fry the seeds in a mud vessel .
2. Siru nerunjil vithai (Tribulus *terrestris,* Linn)
    a. Part used :Seed
    b. Dry the seed in shade and powder it.
3. Thaneer vittan (Asparagus *racemosus,*Wild.)
    a. Part used: Root tuber
    b. Wash the root tuber with running water and dry it.
4. Mullilavu ver (Bombax *malabaricum,*Dc.)
    a. Part used :Root
    b. Dry the root in shade and powder it.
5. Nelli ver (Phyllanthus *emblica,*Linn.)
    a. Part used : Root
    b. Dry the root in shade and powder it.
6. Seenthil sarkarai (Tinospora *cordifolia,*Wild.)
    a. Part used : Stem
    b. Mix well in water, filter it and dry in sunlight.

PREPARATION: All the ingredients were taken in the right proportion in a pestel mortar, ground and filtered as fine powder.

DRUG STORAGE : The trial drug "POONAIKALI VITHAI CHOORANAM " (internal) was stored in a clean and dry wide mouthed glass bottles.

DISPENSING:

The chooranam was dispensed in sachet

Quantity of Medicine A packet of 24 sachets for 12 days each sachets consist of 6 gm.

MUCUNA PRURIENS

Family : Fabaceae

Plant description: Twining herbs, branches terete, striate, downy pubescent. Leaves trifoliate, leaves ovate-rhomboid,apprised white-pubescent. Flowers dark purple with yellow shade on the petal in long axillary racemes. Pods curved, prominently s- shape,densely silk pubescent with persistent pale brown or gray irritant bristles,seeds 4-6, orbicular.

Geographical distribution :

World :Cultivated in Tropics

India : occasionally in damp places, bushes, hedges and ravines throughout India.

Vernacular names: Sanskrit: Atma gupta, hindi: kivach, kan : Turachi- gida, telgu: Dulagondi, Tamil : Poonai kali.

Trade name : Common cowitch

பூனைக்காலி

தழுதாளைநாற் றத்தோடு சாரிரத்தப் போக்கும்
பழுதுபுரி கின்றகரப் பானும் - அழுதேகுந்
தாலமிசை விந்துவுமாஞ் சாற்றற் கரும்பூனைக்
காலி விதையைக் கழறு.

- அகத்தியர் குணவாகடம்

- Taste - Astringent.
- Potency - Moderate.
- Division - Sweet.
- Part used- Seed.
- Action- Nervine tonic, Aphordisiac

Medicinal uses:

- Traditionally in India the seeds of Mucuna pruriens are used as a tonic and aphrodisiac for male virility.
- Seeds are highly reputed medicine for curing Parkinson's disease.
- It is used in fracture healing.
- It is used as anti depressant drug.
- The pods are anthelmintic
- The seeds are anti- inflammatory
- The hairs are used as vermifuge

Tribulus terrestris :

Syn: Tribulus lanuginosus L

Tribulus maximus var.roseus kuntze

Family: Zygophyllaceae

Plant description: The nutlets are hard and bear to four sharp spines, 10mm(0.39) long and 4-6mm(0.16-0.24) broad point to point. These nutlets strikingly resembles goats' or bulls' heads.

Geographical distribution:

World: Native to Southern Asia.

India: Forests throughout India.

Names: goat's-head,bindii, bullhead, burra gokharu, bhakhdi, caltrop,small caltrops,cat's-head,devil's eyelashes, devil's-thorn, devil's-weed,puncture vine, puncturevine, and tackweed.

Trade name : Gokhru

சிறுநெருஞ்சில்

செப்புநெ ருஞ்சில் திரிதோடம் பொக்கிடும்
வெப்பு முதலனைத்தும் வீட்டுங்காண்-செப்பரிய
சுக்கிலமே கம்போர்க்குந் தொல்லையனல் மாற்றும்
மிக்கு மருந்துநீ வீள்.

-அகத்தியர் குணவாகடம்

Taste- Astringent,sweet potency - Moderate, class - sweet.

Action: Aphrodisiac

Medicinal uses:

- Tribulus seems to work by increasing the level of luteinzing hormones.this hormones sends a signal through the body to start producing testosterone.
- The popularity of tribulus as an herbal remedy for erectile dysfunction.

Research papers: The diuretic properties of TT are due to large quantities of nitrates and essential oil present in its fruits and seeds. (Divya kanchan 2003) plant Med.53:8- 2003.

Asparagus racemosus Willd.

Family: Liliaceace

Plant description: perennial armed climbing shrub. Roots tuberous. Stem angular. Leaves scaly.cladodes 2-6 in whorl, linear, falcate. Flowers white in racemes. Fruit berry, globose, red when ripe 3-6 seeded.

Geographical distribution:

World: south Asia, China, Malaysia, and Australia.

India : occasional in forests all over India.

Names: sana: satavari Guj:Ekalakanto,Shatavari; Hind : Chatwal, kan: Aheruballi,mal: Shatavalli,Mar:Zatar, Tamil: Kilvari,Catavari; tel:Pilligadallu.

Trade name : Wild Asparagus.

தண்ணீர்விட்டான்

நீரிழிவைப் போக்கும் நெடுநாட்சு ரத்தையெலாம்
ஊரைவிடுத் தோடவு ரைக்குங்காண்-நாரியாரே! ஆ
வெண்ணீர்பெய்சோமநோய்வெட்டையணல்தணிக்குந்
தண்ணீர்விட் டான்கிழங்குக் தான்.

-அகத்தியர்குணவாகடம்

- Taste -Sweet.
- Potency - Moderate.
- Division - Sweet.
- Part used- leaves.

Action- Aphrodisiac, Nutritive,Antispasmodic.

Medicinal uses:

- The root is used in indigenous medicine.
- It is considered aphrodisiac and demulcent.
- It is prescribed for increasing the secretion of milk
- The root is used to cure tuberculosis, leprosy, skin diseases, inflammations

RESEARCH PAPERS: 1. Methanolic extract of fresh roots showed gastroduodenal ulcer protective activity (Sairam et al., 2003)

Bombax Malabaricum:

Syn: Bambax ceiba.f.

Bambax heptaphyllum Cav.

Family: Bombacaceae

Plant description: Bombax species are among the largest tree in their regions,reaching 30 to 40 meteres in height and up to 3 meteres trunk diameter.

Geographical distribution:

World: Native to western Africa.

India: Forests throughout India.

Names: Silk cotton tree, simal, red cotton tree, kapok, and simply bombax. In Chinese they are known as Mumian.

Trade name : kapok tree.

முள்இலவு

தந்துமே கஞ்சிறுநீர்த் தாரைவெப் பம்வாயு
வுந்தவரு பேதியிவை யோட்டுங்காண்- முந்திக்
கிளர்வள்ளை பாயும்வரிக் கெண்டை விழியாய்
வளர்முள் ளிலவு மரம்.

- அகத்தியர் குணவாகடம்

Taste- Astringent,sweet potency - Moderate, class -sweet.

Action: Aphrodisiac

Medicinal uses:

- The roots are valuable as an aphrodisiac and to prevent premature ejaculation.
- The mashed roots with nutmeg powder are an effective adjuvant in diabetes.

Research papers: The extract of stem bark of Bombax ceiba has significant anti-obesity potential against HFD induced experimental obesity, possibly due to modulation of FAS and PTP-1B signaling in Wistar rats due to the presence of active flavanoids and lupeol respectively. Verma Rameshwar*, Devre Kishor, GangradeTushar ,Gore Siddharth, Gour Sudarshan G.R.Y. Institute of Pharmacy, Vidhya vihar, Borawan (Khargone), M.P.-451228, India.

Phyllanthus emblica:

Syn: Emblica arborea Raf.

Emblica officinalis Gaertn.

Family: Phyllanthaceae

Plant description: The tree is small to medium in size, reaching 1–8 m (3 ft 3 in–26 ft 3 in) in height. The branchlets are not glabrous or finely pubescent, 10–20 cm (3.9–7.9 in) long**.**The fruit is nearly spherical, light greenish yellow, quite smooth and hard on appearance, with six vertical stripes or furrows.

Geographical distribution:

World: Large area ranging from Nepal and Sri Lanka .

India: Forests throughout India.

Names: *Phyllanthus emblica*, also known as emblic, emblic myrobalan, myrobalan, Indian gooseberry, Malacca tree, or amla from Sanskrit amalika

Trade name : Amla/ Emblica Officinalis/ Indian Gooseberry

நெல்லி
வமனம் அரோசியறும் வாதமுதன் மூன்றுஞ்
சமன முறுமலமுஞ் சாறும்-அமானசுரம்
புல்லிவரு தோடசன்னி பொல்லாச் செயலும் போம்
நெல்லிமர வேரை நினை.

- அகத்தியர் குணவாகடம்

Taste- Sour,Astringent,Sweet potency - Moderate, class – sweet.

Action: Aphrodisiac

Medicinal uses:

- As an extremely rich source of vitamin C, Indian gooseberry is one of the best remedy for scurvy.
- It also balance both pitha and vaatha by virtue of its sweet taste. The kapha is balanced primarily due to its drying action.

Research papers: There is Preliminary evidence in vitro that extract of P.emblica induce apoptosis and modify gene expression in osteoclasts.(Penolazzi.l,Lampronti I, Borgatti.M (2008).

Tinospora cordifolia:

Syn: Tinospora baenzigeri Foramen

Tinospora capillipes Gagnep.

Family: Menispermaceae

Plant description: It is a large, deciduous extensively spreading climbing shrub with several elongated twining branches. Leaves simple, alternate, exstipulate, long petioles up to 15 cm long, roundish, pulvinate, both at the base and apex with the basal one longer and twisted partially and half way around.

Geographical distribution:

World: Native to tropical area of Myanmar,and Sri Lanka.

India: Throughout tropical region of India.

Names: Heart leaved, Moon seed , guduchi, giloy

Trade name : Giloy

சீந்தில்

மேகமெனு மாதபத்தால் வெந்த வுயிர்ப்பயிரைத்
தாக மடங்கத் தணித்தலால்-ஆகம்
அமர ரெனலிருக்க வாதரித்த லாலே
அமுதவல்லி சஞ்சீவி யாம்.

- அகத்தியர் குணவாகடம்

Taste-Bitter, potency - Hot division, class - pungent.

Action: Aphrodisiac

Medicinal uses:

- The juice or powder of Giloy Stem is useful in treating various type of cancer. Giloy is an immunomodulatory.
- Tinospora cordifolia is a top herbal remedy in preventing Swine Flu.

Research papers: The alcoholic extract of *T. cordifolia* has been found to exert anti-inflammatory actions in models of acute and subacute inflammation . The water-soluble fraction of 95% ethanolic extract of *T. cordifolia* plant has shown significant antipyretic activity.(Avinish k, Upadhyay,Kaushal kumar) internal j Ayurveda Res .Apr-june 2010

Saccharum Officinarum:

Syn: Arundo saccharifera Garsault

Saccharum hybridum R.M.Grey

Family: poaceae (gramineae)

Plant description: *S. officinarum*,a perennial plant, grows in clumps consisting of a number of strong unbranched stems. The stems vary in colour, being green, pinkish, or purple and can reach 5 m (16 ft) in height. They are jointed, nodes being present at the bases of the alternate leaves.

Geographical distribution:

World: It is originated in south Asia

India: First domesticated in India.

Names: Sugar cane, Noble cane, whilt salt

Trade name : Sugarcane.

கற்கண்டு

ஈறின் தடிப்பு மிருமலும்பல் வாந்திகளுஞ்
சீறுகப முட்டினமுஞ் சேராதே-தேறியநற்
சொற்கண் டிளங்குயில்கள் சூழ மடவனமே
கற்கண் டெனவுரைக்குங் கால்.

-அகத்தியர் குணவாகடம்

Taste- Sweet, potency - moderate, class - sweet.

Action: Anti septic, Demulcent

Medicinal uses:

- The juiciest and sweetest sugarcane is the tropical green sugar cane.it strengthens stomach,kidney,heart,eyes,brain and sex organs.
- The sugarcane can be used as simple energizer and protein supplement in infectious fevers.

Research papers: The phenolic extract obtained from sugar cane juice showed a protective effect against in vivo MeHgCl intoxication (Antioxidant activity).(Sepideh Miraj) Der Pharmacia Lettre,2016,8(13):223-225)

Mucuna *pruriens*

Bombax *malabaricum*

Karkandu

Asparagus *racemosus*

Tinospora *cordifolia*

Tribulus *terrestris*

Phyllanthus *emblica*

Ponnaikali vithai chooranam

PROTOCOL

TITLE:

SAFETY AND CLINICAL EVALUATION OF "POONAIKALI VITHAI CHOORANAM" IN THE TREATMENT OF "AAN MALADU" (MALE INFERTILITY)

REG NO: **DATE OF SUBMISSION :**

NAME OF THE INSTITUTION:

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Tambaram Sanatorium,

Chennai-47

Telephone No : 044-22411611

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Department of Maruthuvam,

National Instituite of Siddha,

Chennai - 47.

5. NAME OF THE GUIDE:

Prof.Dr.S.Mohan,.MD(S),

Director and Head of the Department,

Department of Maruthuvam,

National Instituite of Siddha,

Chennai - 47.

BACK GROUND:

In 20th century usage of herbal based medicinal therapy gained importance and found their place in 40% of prescription because of their lesser side effects on par with other chemical drugs. The usage of medicinal plant products in the form of plant extracts and their active components etc.

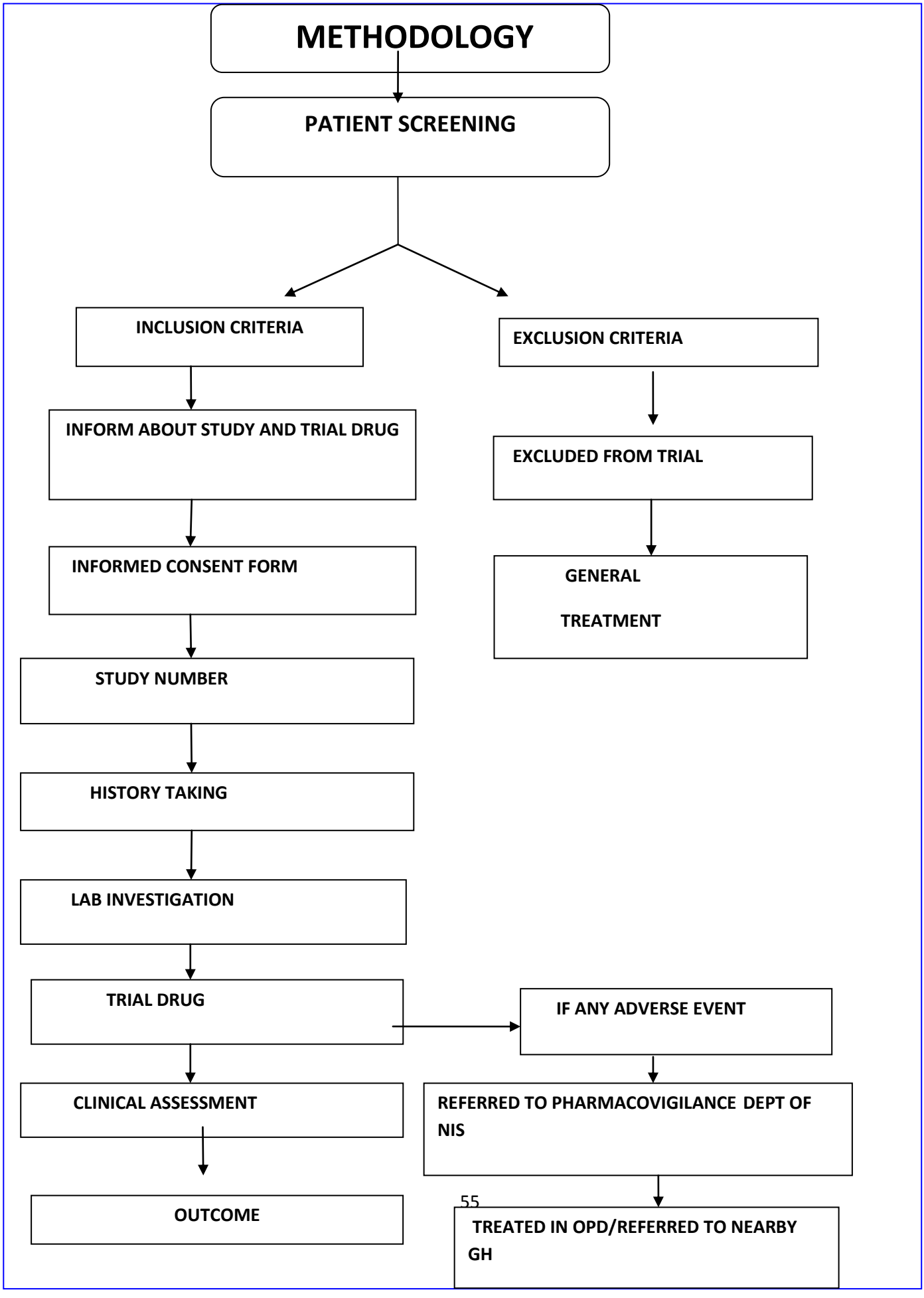
Yugi muni had done a lot of contribution to the siddha system, includes the classification of disease into 4448. AAN MALADU is one among them. According to Yugi muni in Aan maladu the semen exhibits the following characters such as absence of sweetness, buoyancy on water.He further explained the character of urine in Aan maldu as froth in urine and symptoms like absence of virility.

Sukkilam one among the seven udal thathukkal is affected in Aan maladu. Aan maladu is known as male Infertility in modern science . Most cases of male infertility are due to an abnormal sperm,abnormal sperm count and low sperm motility. Infertility is the inability of a sexually active, non contraception couple to achieve pregnancy in one year. As per WHO guidelines a report with count less than 15 million / ml is oligospermia. There was a time when infertility was only limited to women. In present scenario male infertility is blamed in 50 % of cases where couples could not conceive naturally. Male infertility is a global problem in the field of reproductive health. . Infertility bears a social stigma.The incidence of infertility is follows males - 40% females- 40% and both sex -20%. Most of the cases are hailing from IT back ground, chemical industry, oil refineraries, other than occupation viral infection during childhood (ex mumps) endocrine disorder, trauma(testes), ,low economic standards, can also lead to rise in infertility rate.

The research study entitled Aan maldu (Male infertility) mainly focus on outcome of qualitative and quantitative analysis of semen in oligospermia patients with the trial drug poonaikali vithai chooranam . Poonaikali vithai chooranam is a poly herbal compound .The ingredients of poonaikali vithai chooranam are possessing anti oxidants (kayakalpha drugs) and aphrodisiac properties.

Poonaikali vithai(Mucuna *pruriens*), Siru nerunjil vithai (Tribulus *terrestris*), Thanneer vittan kizhangu (Asparagus *racemosus*), Mullilavu ver (Bombax *malabaricum*), Nelli ver (Phyllanthus *emblica*), Seenthil sarkarai (Tinospora *cordifolia*) and, Karkandu podi are included in the trial drug.

Since the trial medicines is yet to be documented for its efficacy, it is essential to do safety studies before going for clinical trial.


METHODOLOGY
PATIENT SCREENING
INCLUSION CRITERIA
EXCLUSION CRITERIA
INFORM ABOUT STUDY AND TRIAL DRUG
EXCLUDED FROM TRIAL
INFORMED CONSENT FORM
GENERAL
TREATMENT
STUDY NUMBER
HISTORY TAKING
LAB INVESTIGATION
TRIAL DRUG
IF ANY ADVERSE EVENT
CLINICAL ASSESSMENT
REFERRED TO PHARMACOVIGILANCE DEPT OF NIS
OUTCOME
TREATED IN OPD/REFERRED TO NEARBY GH

OBJECTIVE :

Primary objective :

To evaluate the therapeutic efficacy of siddha formulation "Poonaikali vithai chooranam" in the treatment of AAN MALADU (male infertility)

Secondary objective:

To evaluate the safety profile (Acute, Sub acute toxicity studies) of the trial drug.To study the siddha cofactors such as age, occupations, socio economic status, dietary influence.etc

STUDY DESIGN & CONDUCT OF STUDY:

Study type : An open clinical trial

Study place : OPD Of Ayothidass pandithar hospital,National Institute of Siddha , Tambaram sanatorium, Chennai-47.

Study period : 12 months

Sample size : 40 patients

TREATMENT:

MEDICINE NAME :

"Poonaikali vithai chooranam"

Ref : GUNAPADAM MOOLIGAI VAGUPU

Author : Vaithiya rathinam K.S Murugesa muthalaiyar: 1st Edison pg no 708 (publication year 1936)

DOSAGE : 6 gm twice a day After food

ADJUVANT : Cow's Ghee

DURATION : 48 days

ROUTE OF DRUG ADMINISTRATION : oral route

STANDARD OPERATING PROCEDURE OF THE TRIAL DRUG -"POONAIKALI VITHAI CHOORANAM"

SOURCE OF RAW DRUGS:

The required raw drugs for the preparation of Poonaikali vithai chooranam will be purchased from a well reputed country shop. The raw drugs will be authenticated by the Asst. Prof of medicinal botany at NIS. Then the raw drugs will be purified as mentioned in siddha literature. The medicine is prepared in Gunapadam lab of National Institute of Siddha.

REQUIRED RAW DRUGS:

1. poonaikali vithai(Mucuna *pruriens,* Linn Dc)
2. Siru nerunjil vithai (Tribulus *terrestris*,Linn)
3. Thanneer vittan kizhangu (Asparagus *racemosus,*Wild)
4. Mullilavu ver (Bombax *malabaricum,*Dc)
5. Nelli ver (Phyllanthus *emblica,*Linn)
6. Seenthil sarkarai (Tinospora *cordifolia,*Wild) and
7. Karkandu podi (Quantity equal to the powder of all the above)

METHOD OF PURIFICATION :

- (Ref :Sigicha Rathina Deepam, Author :C.Kannusamipillai. Edition 2007)

POONAIKALI VITHAI CHOORANAM (Internal)

1.POONAI KALI(Mucuna *pruiens,* Linn Dc)
   a.Part used :Seed
   b.Fry the seeds in a mud vessel .

2.Siru nerunjil vithai (Tribulus *terrestris,* Linn)
   a.Part used :Seed
   b.Dry the seed in shade and powder it.

3.THANEER VITTAN (Asparagus *racemosus*,Wild.)
   a. Part used: Root tuber
   b. Wash the root tuber with running water and dry it.

4.Mullilavu ver (Bombax *malabaricum,*Dc.)
   a. Part used :Root
   b.Dry the root in shade and powder it.

5.Nelli ver (Phyllanthus *emblica,*Linn.)
   a.Part used : Root
   b.Dry the root in shade and powder it.

6.Seenthil sarkarai (Tinospora *cordifolia,*Wild.)

a.Part used : Stem

b.Mix well in water, filter it and dry in sunlight.

PREPARATION:

All the ingredients will be taken in the right proportion in a pestel mortar, grinded and filtered as fine powder.

DRUG STORAGE :

The trial drug "POONAIKALI VITHAI CHOORANAM " (internal) is stored in clean and dry wide mouthed glass bottles.

DISPENSING:

The chooranam will be dispensed in sachet

Quantity of Medicine

A packet of 24 sachets for 12 days each sachets consist of 6 gm.

SUBJECT SELECTION:

As and when patients reporting at OPD of Ayothidass Pandithar Hospital with symptoms mentioned in inclusion criteria will be subjected to screening test & documentation will be done by using screening proforma.

INCLUSION CRITERIA:

1. Male infertile
2. Age 21- 45 year
3. Maritial status - more than 1 year
4. Sperm count $\leq$ 40 million / ejaculation
5. Motility less than $\leq$ 50 %
6. Patient who is willing to sign the informed consent stating that he will continuously stick to the treatment during 48days but can opt out of the trial of his own conscious discretion.
7. Patients who are willing to give specimen of blood , urine and semen before and after treatment.

EXCLUSION CRITERIA

1. Azoospermia
2. Hydrocele
3. Diabetes mellitus
4. Hypertension
5. Endocrine disorders
6. Caridiac diseases
7. VDRL & STD
8. Inguinal Hernia
9. Renal diseases
10. Varicose veins

WITHDRAWAL CRITERIA

1. Intolerance to the drug & development of adverse reactions during drug trial.
2. Poor patient compliance & defaulters.
3. Patient turned unwilling to continue in the course of clinical trial.
4. Increase in severity of symptoms.

TEST & ASSESSMENTS

A. CLINICAL ASSESSMENT

SIDDHA ASSESSMENT

B. ROUTINE INVESTIGATION

C. SPECIFIC INVESTIGATION

A. CLINICAL ASSESSMENT (5)

1. Premature ejaculation
2. Nocturnal emission
3. Erectile dysfunction
4. Painful coitus
5. Painful micturition

SIDDHA ASSESSMENT

1.Thinai :

- Kurinchi (hill areas)
- Mullai (forest)
- Marutham (fertile land)
- Neidhal (coastal area)
- Palai (desert)

2. Paruva Kalam (season)

- Karkaalam (Aug 18 – Oct 17)
- Koothir kaalm (Oct 18 – Dec 16)
- Munpanikaalm (Dec 17 – Feb 12)
- Pinpani kaalam (Feb 13 – April 13)
- Ilavenil kaalam (April 14 – June 14)
- Muthuvenil kaalam (June 15 – Aug 17)

3. Poripulankal:

- Mei (Skin etc)
- Vaai (Tongue etc)
- Kan (Eye etc)
- Mooku (Nose etc)
- Sevi (Ear etc)

6.Ennvagaithervu (Eight types of Examination):

- Naadi
- Sparisam
- Naa
- Niram
- Mozhi
- Vizhi

- Malam
- Moothiram

  - Neerkuri

  - Neikuri

B . ROUTINE INVESTIGATION

- Hb(gm/dl)
- Total WBC Count(cells/cumm)
- DC- Polymorphs(%)
- Lymphocytes(%)
- Eosinophils (%)
- Monocytes (%)
- Basophils(%)
- Total RBC count million cells/cumm)
- ESR(Men 6-12mm/hr Women 7-18 mm/hr)
- B.glucose (mg/dl) F & PP

LIPID PROFILE

- Serum T.cholesterol(mg/dl)-
- HDL cholesterol(mg/dl)-
- LDL cholesterol(mg/dl)-
- VLDL cholesterol(mg/dl)-
- Serum triglycerides (mg/dl)-

KIDNEY FUNCTION TEST

- B.urea(mg/dl)
- S. total creatinine (mg/dl)

LIVER FUNCTION TEST

- S.total bilirubin(mg/dl)
- S.direct bilirubin (mg/dl)
- S. indirect bilirubin (mg/dl)

- SGOT(u/l)
- SGPT (u/l)
- S.alkaline phosphataseu/l)
- S.total protein(g/dl)
- S. albumin (g/dl)
- S.globulin (g/dl)
- S. calcium (mg/dl)
- S. phosphorous (mg/dl)

URINE EXAMINATION

- Albumin
- Sugar (Fasting & post prandial)
- Deposits
- Bile salts
- Bile pigments
- Urobilinogen

SPUTUM - AFB

SPECIFIC INVESTIGATION

Semen analysis –

Volume

Colour

Appearance

Viscosity

Liquification time

Fructose

Sperm count

Motility

Morphology

STUDY ENROLLMENT:

- In this clinical trial patients reporting at NIS OPD with the clinical symptoms of premature ejaculation, Nocturnal emission, Erectile dysfunction, Painful coitus, Painful micturition will be examined clinically for enrolling in the study based on the inclusion and exclusion criteria.
- The patients in this study will be informed (Form-V) about the objective of the study, trial drug, possible outcomes in their own language and terms understandable to them.
- After ascertaining the patient's willingness, informed consent would be obtained in writing from them in the consent form .(Form- VI)
- All these patients will be given unique registration card in which patient's registration number of the study, Address, Phone number and Doctors phone number etc. so as to report easily and if any adverse reactions arise.
- Complete clinical history, complaints and duration, examination findings-- all will be recorded in the prescribed Proforma in the history and clinical assessment forms separately. Screening Form- I will be filled up; Form –II and Form –III will be used for recording the patient's history, clinical examination of symptoms and signs and laboratory investigations respectively.
- Patients would be advised to take the trial drug and appropriate dietary advice (Form IV-D) would be given according to the patients' perfect understanding.

CONDUCT OF THE STUDY:

The trial drug POONAIKALI VITHAI CHOORANAM (Internal) is given for 48 days.

Patients are advised to visit the hospital once in 12 days to get the trial drug. At each clinical visit clinical assessment will be done and prognosis will be noted.

Laboratory investigations & SEMEN ANALYSIS will be done on 0th day & 48 th day of the trial for OP patients .

If any trial patient who fails to collect the trial drug on the prescribed day but wants to continue in the trial from the next day or two, he will be allowed, but defaulters of one week and more will not be allowed to continue and be withdrawn from the study with fresh case being included.

DATA MANAGEMENT

- After enrolling the patient in the study, a separate file for each patient will be opened and all forms will be filed in the file. Study No. and Patient No. will be entered on the top of file for easy identification. Whenever the study patient visits OPD during the study period, the respective patient file will be taken and necessary recordings will be made at the assessment form or other suitable forms.

- The screening forms will be filed separately.

- The Data recordings will be monitored for completion by HOD and adverse event by Sr.Research Officer (Statistics). All forms will be further scrutinized in presence of Investigators by Sr.Research Officer (Statistics) for logical errors and incompleteness of data to avoid any bias. No modification in the results is permitted for unbiased reports.

STATISTICAL ANALYSIS:

All collected data will be entered into the computer and manually cross-checked the correctness of the data entry. The clinical symptoms and labarotary investigation of semen will be analyzed by comparing the two point of data (before and after treatment) paired test and chi-square test will be employed to study the efficacy of treatment. Further, the effect of co factors (age, occupation, socio economic status.etc) will also be statistically analyzed.

OUTCOME

1. PRIMARY OUT COME

Primary Outcome is mainly assessed by increase in the sperm count and motility %

RESULT	SPERM COUNT & MOTILITY (/ ejaculates)	FROM	TO
GOOD	SPERM COUNT *	≤ 40 million	≥ 60 million
	MOTILITY % #(RM+PM)	≤ 50%	≥ 70 %
MODERATE	SPERM COUNT *	≤ 40 million	> 50 million
	MOTILITY % #(RM+PM)	≤ 50%	≥ 60 %
MILD	SPERM COUNT *	≤ 40 million	40-50 million
	MOTILITY % #(RM+PM)	≤ 50%	> 50 %

NOTE:

* As per 1999 WHO criteria (1) standard value for total number of spermatozoa ≥ 40 million per ejaculates.

As per 1999 WHO criteria (1) standard value for motility is ≥ 50 % million per ejaculates.

Progressive motility (PM) - ≥ 50 %

Rapid motility (RM) - 25 %

2. SECONDARY OUT COME

Secondary Out Come is mainly assessed by reduce the clinical symptoms.

ADVERSE EFFECT/SERIOUS EFFECT MANAGEMENT:

If the trial patient develops any adverse reaction. It will be recorded in pharmacovigilence form, and he would be immediately referred to of Pharmacovigilance department of NIS and proper management will be given in OPD of National institute of siddha.

ETHICAL ISSUES

1. Informed consent will be obtained from the patient after explaining about the clinical trial in the understandable language to the patient.
2. The data collected from the patient will be kept confidentially.
3. After getting the consent of the patient in the consent form they will be enrolled in the study
4. Treatment would be provided free of cost.
5. No other external or internal medicines will be used. There will be no infringement on the rights of patient.
6. To prevent any infection, while collecting blood sample from the patient, only disposable syringes, disposable gloves, and needles will be used under proper sterilization cover.
7. The patients who are excluded (as per exclusion citeria) are given proper treatment at National Institute of Siddha
8. In conditions of treatment failure, adverse reactions, patients will be given alternative treatment at the National Institute of Siddha with full care throughout the end of the treatment

ASSESSMENT FORM

FORM I	SCREENING AND SELECTION PROFORMA
FORM II	CLINICAL RESEARCH FORM
FORM lll	LABORATORY INVESTIGATION ON ENROLLMENT AND CONCLUSION OF TRIAL
FORM IV	DRUG COMPLIANCE FORM
FORM V	PATIENT INFORMATION SHEET
FORM VI	PATIENT CONSENT FORM
FORM VII	WITHDRAWAL FORM / ADVERSE REACTION FORM / PHARMACOVIGILENCE FORM
FORM VIII	DIETARY ADVICE FORM

ACUTE ORAL TOXICITY STUDY OF *POONAIKALI VITHAI CHOORANAM*

(OECD GUIDELINE – 423)

Introduction:

- The acute toxic class method is a stepwise procedure with the use of 3 animals of a single sex per step.
- Depending on the mortality and/or the moribund status of the animals, on average 2-4 steps may be necessary to allow judgement on the acute toxicity of the test substance.
- This procedure is reproducible, uses very few animals and is able to rank substances in a similar manner to the other acute toxicity testing methods.
- The acute toxic class method is based on biometric evaluations with fixed doses, adequately separated to enable a substance to be ranked for classification purposes and hazard assessment.
- In principle, the method is not intended to allow the calculation of a precise LD50, but does allow for the determination of defined exposure ranges where lethality is expected since death of a proportion of the animals is still the major endpoint of this test.
- The method allows for the determination of an LD50 value only when at least two doses result in mortality higher than 0% and lower than 100%.
- The use of a selection of pre-defined doses, regardless of test substance, with classification explicitly tied to number of animals observed in different states improves the opportunity for laboratory to laboratory reporting consistency and repeatability.

Principle of the Test:

It is the principle of the test that based on a stepwise procedure with the use of a minimum number of animals per step, sufficient information is obtained on the acute toxicity of the test substance to enable its classification. The substance is administered orally to a group of experimental animals at one of the defined doses. The substance is tested using a stepwise procedure, each step using three animals of a single sex. Absence or presence of compound-related mortality of the animals dosed at one step will determine the next step, i.e.

– no further testing is needed

− dosing of three additional animals, with the same dose

− dosing of three additional animals at the next higher or the next lower dose level. The method will enable a judgment with respect to classifying the test substance to one of a series of toxicity classes.

Methodology:

Selection of Animal Species

The preferred rodent species is the wistar albino rat, although other rodent species may be used. Healthy young adult animals are commonly used laboratory strains should be employed. Females should be nulliparous and non-pregnant. Each animal, at the commencement of its dosing, should be between 6 to 8 weeks old and the weight (150-200gm) should fall in an interval within±20 % of the mean weight of any previously dosed animals.

Housing and Feeding Conditions

The temperature in the experimental animal room should be 22ºC ± 3ºC. Although the relative humidity should be at least 30% and preferably not exceed 70% other than during room cleaning the aim should be 50-60%. Lighting should be artificial, the sequence being 12 hours light, 12 hours dark. For feeding, conventional laboratory diets may be used with an unlimited supply of drinking water. Animals may be group-caged by dose, but the number of animals per cage must not interfere with clear observations of each animal.

Preparation of animals: The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions

Test Animals and Test Conditions:

Sexually mature Female Wistar albino rats (150-200gm) were obtained from TANUVAS,Madhavaram, Chennai. All the animals were kept under standard environmental condition (22±3°C). The animals had free access to water and standard pellet diet (Sai meera foods, Bangalore).

Preparation of animals:

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions

Preparation for Acute Toxicity Studies

Rats were deprived of food overnight (but not water 16-18 h) prior to administration of the, ***Poonaikali vithai choornam***.

The principles of laboratory animal care were followed and the Institutional Animal Ethical Committee approved the use of the animals and the study design

IAEC approved Number: IAEC/XLIX/13/CLBMCP/2016

Test Substance	: **POONAIKALI VITHAI CHOORNAM**
Animal Source	: TANUVAS,Madhavaram, Chennai.
Animals	: Wister Albino Rats (Female-3+3)
Age	**:** 6-8 weeks
Body Weight on Day 0	**:** 150-200gm.
Acclimatization	**:** Seven days prior to dosing.
Veterinary examination	**:** Prior and at the end of the acclimatization period.
Identification of animals	**:** By cage number, animal number and individual marking by using Picric acid.
Number of animals	: 3 Female/group,
Route of administration	: Oral
Diet	**:** Pellet feed supplied by Sai meera foods Pvt Ltd, Bangalore
Water	**:** Aqua guard portable water in polypropylene bottles.
Housing & Environment	**:** The animals were housed in Polypropylene cages provided with bedding of husk.
Housing temperature	**:** between 22ºC ± 3ºC.

Relative humidity **:** between 30% and 70%,

Air changes **:** 10 to 15 per hour and

Dark and light cycle **:** 12**:**12 hours.

Duration of the study **:** 14 Days

Administration of Doses:

Poonaikali vithai choornam was suspended in water and administered to the groups of wistar albino rats in a single oral dose by gavage using a feeding needle. The control group received an equal volume of the vehicle. Animals were fasted 12 hours prior to dosing. Following the period of fasting, the animals were weighed and then the test substance was administered. Three Female animals are used for each group. The dose level of 5, 50, 300 and 2000 mg/kg body weight was administered stepwise. After the substance has been administered, food was withheld for a further 3-4 hours. The principle of laboratory animal care was followed. Observations were made and recorded systematically and continuously as per the guideline after substance administration. The visual observations included skin changes, mobility, aggressively, sensitivity to sound and pain, as well as respiratory movements. Finally, the number of survivors was noted after 24 hrs and these animals were then monitered for a further 14 days and observations made daily. The toxicological effect was assessed on the basis of mortality.

Observations:

Animals are observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days, except where they need to be removed from the study and humanely killed for animal welfare reasons or are found dead. It should be determined by the toxic reactions, time of onset and length of recovery period, and may thus be extended when considered necessary. The times at which signs of toxicity appear and disappear are important, especially if there is a tendency for toxic signs to be delayed. All observations are systematically recorded with individual records being maintained for each animal.

Observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhoea,

lethargy, sleep and coma. The principles and criteria summarized in the Humane Endpoints Guidance Document taken into consideration. Animals found in a moribund condition and animals showing severe pain or enduring signs of severe distress was humanly killed. When animals are killed for human reasons or found dead, the time of death was recorded.

Acute oral toxicity study of *Poonaikali vithai choornam*

Table 1: Dose finding experiment and its behavioral Signs of acute oral Toxicity

Observation done:

SL	Group CONTROL	Observation	SL	Group TEST GROUP	Observation
1	Body weight	Normal	1	Body weight	Normally increased
2	Assessments of posture	Normal	2	Assessments of posture	Normal
3	Signs of Convulsion Limb paralysis	Normal	3	Signs of Convulsion	Absence of sign (-)
4	Body tone	Normal	4	Body tone	Normal
5	Lacrimation	Normal	5	Lacrimation	Absence
6	Salivation	Normal	6	Salivation	Absence
7	Change in skin color	No significant color change	7	Change in skin color	No significant color change
8	Piloerection	Normal	8	Piloerection	Normal
9	Defecation	Normal	9	Defecation	Normal
10	Sensitivity response	Normal	10	Sensitivity response	Normal

11	Locomotion	Normal	11	Locomotion	Normal
12	Muscle gripness	Normal	12	Muscle gripness	Normal
13	Rearing	Mild	13	Rearing	Mild
14	Urination	Normal	14	Urination	Normal

Behaviour:

The animals will be observed closely for behaviour in the first four hours which includes abnormal gait, aggressiveness, exophthalmos, ptosis, akinesia, catalepsy, convolusion, excitation, head twitches, lacrimation, loss of corneal reflex, loss of traction, piloerection reactivity of touch, salivation, scratching, sedation, chewing, head movements, sniffing, straub, tremor and writhes, diarrhea, leathery, sleep and coma.

Body Weight:

Individual weight of animals was determined before the test substance was administered and weights will be recorded at day 1, 7, and 14 of the study. Weight changes were calculated and recorded. At the end of the test, surviving animals were weighed and humanly killed.

Food and water Consumption:

Food and water consumed per animal was calculated for control and the treated dose groups.

Mortality:

Animals were observed for mortality throughout the entire period.

Results:

All data were summarized in tabular form, (Table-1-4) showing for each test group the number of animals used, the number of animals displaying signs of toxicity, the number of animals found dead during the test ,description of toxic symptoms,, weight changes, food and water intake.

No of animals in each group:3

Table 2 (Observational study Results)

No	Dose mg/kg	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1.	**Control**	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2.	**2000mg**	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-

1..Alertness 2. Aggressiveness 3. Pile erection 4. Grooming 5. Gripping 6. Touch Response 7. Decreased Motor Activity 8. Tremors 9. Convulsions 10. Muscle Spasm 11. Catatonia 12. Muscle relaxant 13. Hypnosis 14. Analgesia 15.Lacrimation 16. Exophthalmos 17. Diarrhea 18. Writhing

19. Respiration 20. Mortality.

(+ Present, - Absent)

Table 3 (Body weight Observation)

DOSE	DAYS		
	1	7	14
CONTROL	210.6±31.474	211.2 ± 14.162	220.2 ± 24.22
HIGH DOSE	220.5± 27.75	221.4 ± 3.22	224.1 ± 12.72
P value (p)*	NS	NS	NS

Table 3 (Water intake (ml/day) of Wistar albino rats group exposed to *Poonaikali vithai choornam):*

DOSE	DAYS		
	1	6	14
CONTROL	54 ± 2.22	53±7.42	58.4±2.54
HIGH DOSE	62.2±1.21	62.8±4.46	64.6±2.22
P value (p)*	NS	NS	NS

N.S- Not Significant, **($p > 0.01$), *($p > 0.05$), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 4: Food intake (gm/day) of Wistar albino rats group exposed to *Poonaikali vithai choornam*

DOSE	DAYS		
	1	7	14
CONTROL	45.24±6.32	45.2±6.32	45.4±4.16
High DOSE	42.2±1.44	44.8±2.32	46.1±4.14

REPEATED DOSE 28-DAY ORAL TOXICITY STUDY OF *POONAIKALI VITHAI CHOORNAM*

Test Substance : **Poonaikali vithai choornam**

Animal Source : TANUVAS,Madhavaram, Chennai.

Animals : Wister Albino Rats (Male -24, and Female-24)

Age **:** 6-8 weeks

Body Weight **:** 150-200gm.

Acclimatization **:** Seven days prior to dose.

Veterinary examination **:** Prior and at the end of the acclimatization period.

Identification of animals **:** By cage number, animal number and individual marking by using Picric acid

Diet **:** Pellet feed supplied by Sai meera foods Pvt Ltd, Bangalore

Water **:** Aqua guard portable water in polypropylene bottles.

Housing & Environment **:** The animals were housed in Polypropylene cages provided with bedding of husk.

Housing temperature **:** between 22ºC $\pm$ 3ºC.

Relative humidity **:** between 30% and 70%,

Air changes **:** 10 to 15 per hour

Dark and light cycle **:** 12**:**12 hours.

Duration of the study **: 28 Days.**

Table 5

Groups	**No of Rats**
Group I Vehicle control (Water)	12(6male,6 female)
Group II PVCM- low dose X (20mg)	12 (6male,6 female)
Group III PVCM- Mid dose 10X (200mg)	12 (6male,6female)
Group IV PVCM- High dose 20X(400 mg)	12(6male,6female)

Methodology

Randomization, Numbering and Grouping of Animals:

48 Wistar Albino Rats (24M + 24F) were selected and divided into 4 groups. Each group consist of 12 animals (Male -6, and Female-6). First group treated as a control and other three group were treated with test drug (low, mid, high) for 28 days. Animals were allowed acclimatization period of 7 days to laboratory conditions prior to the initiation of treatment. Each animal was marked with picric acid. The females were nulliparous and non-pregnant.

Justification for Dose Selection:

As per OECD guideline three dose levels were selected for the study. They are low dose (X), mid dose dose (10X), high dose (20X). X is calculated by multiplying the therapeutic dose (30 ml) and the body surface area of the rat (0.018). i.e X dose is (20MG), 10X dose is 200mg/animal,20X dose is 400mg/animal.

Preparation and Administration of Dose:

Poonaikali vithai choornam suspended in with water, It was administered to animals at the dose levels of X, 10X, 20X. The test substance suspensions were freshly prepared every two days once for 28 days. The control animals were administered vehicle only. The drug was administered orally by using oral gavage once daily for 28 consecutive days.

Observations:

Experimental animals were kept under observation throughout the course of study for the following:

Body Weight:

Weight of each rat was recorded on day 0, at weekly intervals throughout the course of study.

Food and water Consumption:

Food and water consumed per animal was calculated for control and the treated dose groups.

Clinical signs:

All animals were observed daily for clinical signs. The time of onset, intensity and duration of these symptoms, if any, were recorded.

Mortality:

All animals were observed twice daily for mortality during entire course of study.

Necropsy:

All the animals were sacrificed by excessive anaesthesia on day 29. Necropsy of all animals was carried out.

Laboratory Investigations:

Following laboratory investigations were carried out on day 29 in animals fasted over-night. Blood samples were collected from orbital sinus using sodium heparin (200IU/ml) for Bio chemistry and potassium EDTA (1.5 mg/ml) for Hematology as anticoagulant. Blood samples were centrifuged at 3000 r.p.m. for 10 minutes.

Haematological Investigations:

Haematological parameters were determined using Haematology analyzer.

Biochemical Investigations:

Biochemical parameters were determined using auto-analyzer.

Histopathology:

Control and highest dose group animals will be initially subjected to histopathological investigations. If any abnormality found in the highest dose group than the low, then the mid dose group will also be examined. Organs will be collected from all animals and preserved in 10% buffered neutral formalin for 24 h and washed in running water for 24 h. The organ sliced 5 or 6µm sections and were dehydrated in an auto technicon and then cleared in benzene to remove absolute alcohol. Embedding was done by passing the cleared samples through three cups containing molten paraffin at 50°C and then in a cubical block of paraffin made by the "L" moulds. It was followed by microtome and the slides were stained with Haematoxylin-eosin red.

Statistical analysis: Findings such as body weight changes, water and food consumption, hematology and blood chemistry

were subjected to One-way ANOVA followed by dunnet t test using a computer software programme – Graph pad version 7.All data were summarized in tabular form, (Table-6 to 12)

RESULTS

Repeated Dose 28- day oral toxic study of Poonaikali vithai choornam

Table 6: Body weight of wistar albino rats group exposed to *Poonaikali vithai choornam*

DOSE	DAYS				
	1	7	14	21	28
CONTROL	260.4±12.42	261.4 ± 20.14	261.7 ± 19.60	262.6 ± 19.16	262.4 ± 12.12
LOW DOSE	240.2 ± 10.12	240.7 ± 38.24	241.4± 42.14	243 ± 52.16	242.42± 12.54
MID DOSE	196.4± 08.74	196.3 ± 12.14	196.2 ± 88.14	198.1 ± 13.66	199.4 ± 22.10
HIGH DOSE	207.6± 16.84	207.8 ± 12.42	208.4 ± 22.26	208 ± 24.18	209 ± 56.41
P value (p)*	NS	NS	NS	NS	NS

NS- Not Significant, **(p > 0.01),*(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 7: Water intake (ml/day) of Wistar albino rats group exposed to *Poonaikali vithai choornam*

DOSE	DAYS				
	1	6	14	21	28
CONTROL	55.9 ± 9.72	56±8.22	57.2±2.20	59±2.16	59.4±2.16
LOW DOSE	58.2±1.21	58.8±3.22	58.9±1.62	60.2±1.28	60.8±1.23
MID DOSE	62.2±2.12	62.3±1.12	63.1±2.422	63.4±1.14	68.4±1.32
HIGH DOSE	64.1±1.21	64.2±1.24	64.4±1.14	64.6±1.42	66.8±2.52
P value (p)*	NS	NS	NS	NS	NS

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 8: Food intake (gm/day) of Wistar albino rats group exposed to *Poonaikali vithai choornam*

DOSE	DAYS				
	2	7	23	22	28
CONTROL	27±5.14	28.5±2.12	29.5±2.17	28.5±1.18	27±2.16
LOW DOSE	29.7±1.18	29.3±1.41	30.1±1.16	30.4±1.21	31.6±1.42
MID DOSE	37.2±2.44	37.2±3.60	37.2±4.25	38.2±2.18	38.2±1.44
HIGH DOSE	29.1±1.14	29.1±1.24	29.6±2.16	29.2±1.20	29.6±3.32
P value (p)*	NS	NS	NS	NS	NS

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test

Table 9: Haematological parameters of Wistar albino rats group exposed to *Poonaikali vithai choornam*

Category	Control	Low dose	Mid dose	High dose	P value (p)*
Haemoglobin(g/dl)	14.8±0.58	14.80±0.64	15.4±0.66	15.18±0.44	N.S
Total WBC (×10^3 l)	7.91±0.52	7.25±0.16	7.48±0.17	7.20±1.32	N.S
Neutrophils (%)	30.25±0.04	31.22±0.12	32.10±1.32	33.06±1.20	N.S
lymphocyte (%)	61.14±1.42	60.12±2.10	60.10±2.22	60.40±2.26	N.S
Monocyte (%)	1.86±0.07	1.85±0.09	1.66±0.03	1.81±0.06	N.S
Eosinophil (%)	0.62±0.04	0.65±0.02	0.66±0.01	0.63±0.06	N.S

Platelets cells10^3/µl	786.14±4.42	788.41±4.16	783.13±7.0	787.16±6.74	N.S
Total RBC 10^6/ µl	6.88±0.12	6.86±0.46	6.62±0.44	6.15±0.22	N.S
PCV%	47.56±0.6	47.46±1.13	48±1.28	47.80±2.24	N.S
MCHC g/dL	34.4±1.32	34.6±1.28	34.28±1.20	34.33±1.12	N.S
MCV fL(µm^3)	52.07±3.24	52.20±1.21	53.10±1.34	54.24±1.42	N.S

N.S- Not Significant, **($p > 0.01$), *($p > 0.05$), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 10 :Biochemical Parameters of of Wistar albino rats group exposed to *Poonaikali vithai choornam*

BIOCHEMICAL PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
GLUCOSE (R) (mg/dl)	80.24±10.6	80.16±6.14	81.22±14.10	81.62±10.2	N.S
T.CHOLOSTEROL(mg/dl)	128.16±1.42	129.25±1.22	126.82±1.28	126.22±1.83	N.S
TRIGLY(mg/dl)	58.36±1.42	58.32±1.28	59.56±1.32	59.66±1.23*	N.S
LDL	81.6±2.53	83.14±2.34	83±2.42	83.44±14.15	NS
VLDL	16.2±2.34	16.42±4.44	16.44±8.24	16.34±24.26	NS
HDL	30.16±6.18	30.26±2.25	32.28±4.26	34.48±20.12	NS
Ratio 1(T.CHO/HDL)	4.12±2.16	4.16±2.14	4.14±2.24	4.26±2.20	NS
Ratio 2(LDL/HDL)	2.70±1.18	2.74±2.12	2.76±3.10	2.76±18.02	NS
Albumin (g/dL)	4.3±0.26	4.63±0.42	4.64±12.42	4.72±15.68	NS

NS- Not Significant, **($p > 0.01$), * ($p > 0.05$), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 11: Renal function test of of Wistar albino rats group exposed to *Poonaikali vithai choornam*

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
UREA (mg/dl)	23.32±0.99	24.28±0.46	24.16±1.28	24.68±1.22	N.S
CREATININE(mg/dl)	0.62±0.08	0.61±0.04	0.62±0.06	0.64±0.08	N.S
BUN(mg/dL)	17.1±0.13	17.10±0.80	17±0.42	17.47±1.12	NS
URIC ACID(mg/dl)	6.22±0.34	6.11±0.22	6.72±0.24*	6.42±0.26	N.S

NS- Not Significant, **(p > 0.01), * (p >0.05) , n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

Table 12: Liver Function Test of of Wistar albino rats group exposed to *Poonaikali vithai choornam*

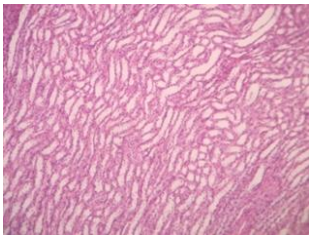
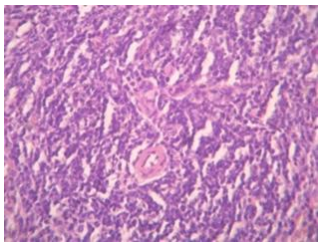
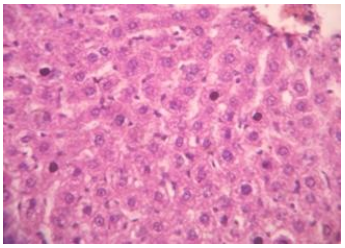
PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
T BILIRUBIN(mg/dl).	0.06±0.06	0.05±0.08	0.6±0.06	0.6±0.04	N.S
SGOT/AST(U/L)	119.15±1.32	119.34±0.52	120.01±1.22	119.75±1.03	N.S
SGPT/ALT(U/L)	70.13±2.18	70.21±1.44	70.14±1.28	71.12±0.48	N.S
ALP(U/L)	133.52±4.26	134±12.14	135.12±14.04*	134.23±12.25*	N.S
T.PROTEIN(g/dL)	7.72±0.36	7.78±0.32	7.76±0.24	7.53±0.48	N.S

NS- Not Significant, **(p > 0.01), * (p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)

HISTO PATHOLOGY

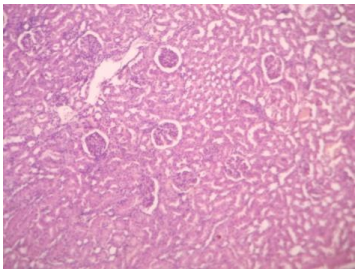
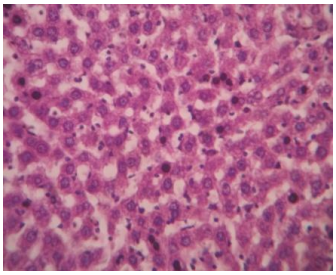
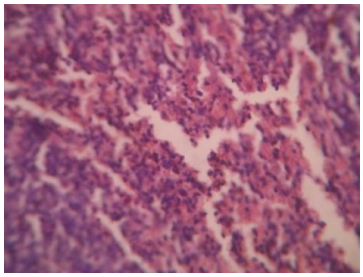
CONTROL GROUP

Kidney Spleen Liver

TEST GROUP (HIGH DOSE)

Kidney Liver Spleen

BIO -CHEMICAL ANALYSIS OF POONAIKALI VITHAI CHOORNAM ANALYSED AT NATIONAL INSTITUTE OF SIDDHA

S.No	EXPERIMENT	OBSERVATION	INFERENCE
1.	Appearance of sample	Brown in colour	
2.	**Solubility:** a. A little(500mg) of the sample is shaken well with distilled water. b. A little(500mg) of the sample is shaken well with con. HCl/Con. H_2So_4	Sparingly soluble	Absence of silicate
3.	**Action of Heat:** A small amount(500mg) of the sample is taken in a dry test tube and heated gently at first and then strong.	No White fumes evolved	Absence of Carbonate
4.	**Flame Test:** A small amount(500mg) of the sample is made into a paste with con. HCl in a watch glass and introduced into non-luminous part of the Bunsen flame.	No Bluish green flame appeared.	Absence of Copper
5.	**Ash Test:s** A filter paper is soaked into a mixture of sample and dil. cobalt nitrate solution and introduced into the Bunsen flame and ignited	No Yellow colour flame	Absence of sodium

Preparation of Extract: 5gm Of **POONAKALI VITHAI CHOORNAM** is weighed accurately and placed in a 250ml clean beaker and added with 50ml of distilled water. Then it is boiled well for about 10 minutes. Then it is cooled and filtered in a 100ml volumetric flask and made up to 100ml with distilled water.

S.No	EXPERIMENT	OBSERVATION	INFERENCE
	I.Test For Acid Radicals		
1.	**Test For Sulphate:** a.2ml of the above prepared extract is taken in a test tube to this added 2ml of 4% dil ammonium oxalate solution	Cloudy appearance present	Absence of **Sulphate**
2.	**Test For Chloride:** 2ml of the above prepared extracts is added with 2ml of dil-HCl is added until the effervescence ceases off..	cloudy appearance present	Presence of **Chloride**
3.	**Test For Phosphate:** 2ml of the extract is treated with 2ml of dil.ammonium molybdate solution and 2ml of con.HNo3	Yellow appearance present	Absence of **Phosphate**
4.	**Test For Carbonate:** 2ml of the extract is treated with 2mldil. magnesium sulphate solution	Presence Cloudy appearance	Presence of **carbonate**
5.	**Test For Nitrate:** 1gm of the substance is heated with copper turning and concentrated H2So4 and viewed the test tube vertically down.	No Brown gas is evolved	Absence of Nitrate
6.	**Test For Sulphide:** 1gm of the substance is treated with 2ml of con. HCL	No Rotten Egg Smelling gas evolved	Presence of Sulphide
7.	**Test For Fluoride & Oxalate:** 2ml of extract is added with 2ml of dil. Acetic acid and 2ml dil.calcium chloride solution and heated**.**	Presence Cloudy appearance	Presence of **fluoride and oxalate**
8.	**Test For Nitrite:** 3drops of the extract is placed on a filter paper, on that-2 drops of dil.acetic acid and 2 drops of	No Characteristic changes	Absence of Nitrite

	dil.Benzidine solution is placed.		
9.	**Test For Borate:** 2 Pinches(50mg) of the substance is made into paste by using dil.sulphuric acid and alcohol (95%) and introduced into the blue flame.	Bluish green colour flame not appeared	Absence of borate

	II. Test For Basic Radicals		
1.	**Test For Lead:** 2ml of the extract is added with 2ml of dil.potassium iodine solution.	NoYellow Precipitate is obtained.	Absence of Lead
2.	**Test For Copper:**One pinch(50mg) of substance is made into paste with con. HClin a watch glass and introduced into the non-. luminuous part of the flame	No Blue colour flame No Blue colour precipitate formed.	Absence of copper
3.	**Test For Aluminium:** To the 2ml of extract dil.sodium hydroxide is added in 5 drops to excess.	No Yellow colour appeared	Absence of aluminium
4.	**Test For Iron:** a.To the 2ml of extract add 2ml of dil.ammonium solution b. To the 2ml of extract 2ml thiocyanate solution and 2ml of con HNo3 is added	No red colour appear	Presence of Iron
5.	**Test For Zinc:** To 2ml of the extract dil.sodium hydroxide solution is added in 5 drops to excess and dil.ammonium chloride is added.	White precipitate is not formed	Absence of Zinc
6.	**Test For Calcium:** 2ml of the extract is added with 2ml of 4% dil.ammonium oxalate solution	No Cloudy appearance and white precipitate	Presence of calcium
7.	**Test For Magnesium:** To 2ml of extract dil.sodium hydroxide solution is added in drops to excess.	No White precipitate is obtained	Presence of Magnesium

8.	**Test For Ammonium:** To 2ml of extract 1 ml of Nessler's reagent and excess of dil.sodium hydroxide solution are added.	No Brown colour appeared	Presence of ammonium
9.	**Test For Potassium:** A pinch(25mg) of substance is treated of with 2ml of dil.sodium nitrite solution and then treated with 2ml of dil.cobalt nitrate in 30% dil.glacial acetic acid.	No Yellowish precipitate is obtained.	Presence of Potassium

10.	**Test For Sodium**: 2 pinches(50mg) of the substance is made into paste by using HCl and introduced into the blue flame of Bunsen burner.	No yellow colour flame appeared	Absence of sodium
11.	**Test For Mercury**: 2ml of the extract is treated with 2ml of dil.sodium hydroxide solution.	No yellow precipitate is obtained	Absence of mercury
12.	**Test For Arsenic:** 2ml of the extract is treated with 2ml of dil.sodium hydroxide solution.	No brownish red precipitate is obtained	Absence of arsenic
	III. Miscellaneous		
1.	**Test For Starch:** 2ml of extract is treated with weak dil.iodine solution	blue colour developed	presence of starch
2.	**Test For Reducing Sugar:** 5ml of Benedict's qualitative solution is taken in a test tube and allowed to boil for 2 minutes and added 8 to 10 drops of the extract and again boil it for 2 minutes. The colour changes are noted.	Brick red colour not developed	Absence of reducing sugar
3.	**Test For The Alkaloids**: a) 2ml of the extract is treated with 2ml of dil.potassium lodide solution. b) 2ml of the extract is treated with 2ml of dil.picric acid. c) 2ml of the extract is treated with 2ml of dil.phosphotungstic acid.	No Yellow colour developed	Presence of Alkaloid
4.	**Test For Tannic Acid:** 2ml of extract is treated with 2ml of dil.ferric chloride solution	No black precipitate is obtained	Absence of Tannic acid
5.	**Test For Unsaturated Compound:** To the 2ml of extract 2ml of dil.Potassium permanganate solution is added.	Potassium permanganate is decolourised	Absence of unsaturated compound

6.	**Test For Amino Acid:** 2 drops of the extract is placed on a filter paper and dried well. 20ml of Biurette reagent is added**.**	violet colour developed	Absence of amino acids
7.	**Test For Type Of Compound:** 2ml of the extract is treated with 2 ml of dil.ferric chloride solution.	No green colour developed No red colour developedNo violet colour developed No blue colour developed	Absence ooxyquinole pinephrine and pyro catechol Antipyrine, Aliphatic amino acidsand meconic acid are absent Apomorphine salicylate and Resorcinol areabsent.

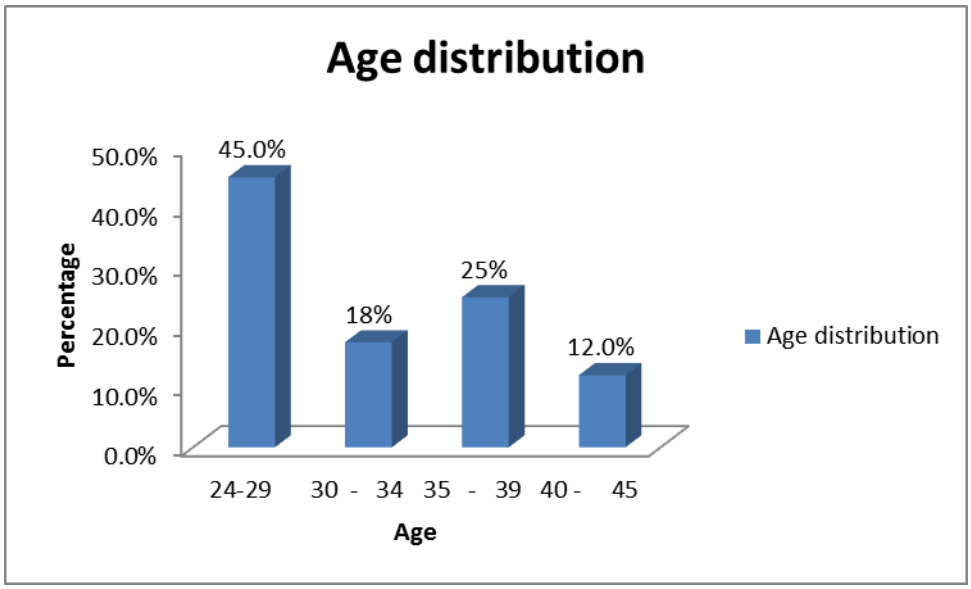
OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

Table-1 Age Distribution

Age (yrs)	Cases	
	No	Percentage (%)
24 - 29	8	45
30 - 34	16	18
35 - 39	12	25
40 - 45	4	12
Total	40	100

Chart-1:



2) Occupational Status

Sl. No	Nature of Work	No. of Cases	Percentage
1	IT Profession	3	7.5%
2	Jobless	5	12.5%
3	Electrician	15	37.5%
4	Businessman-Privately owned	6	15%
5	Coolie	3	7.5%
6	Tailor	2	5%
7	Army	1	2.5%
8	Building workers	2	5%
9	Driver	3	7.5%

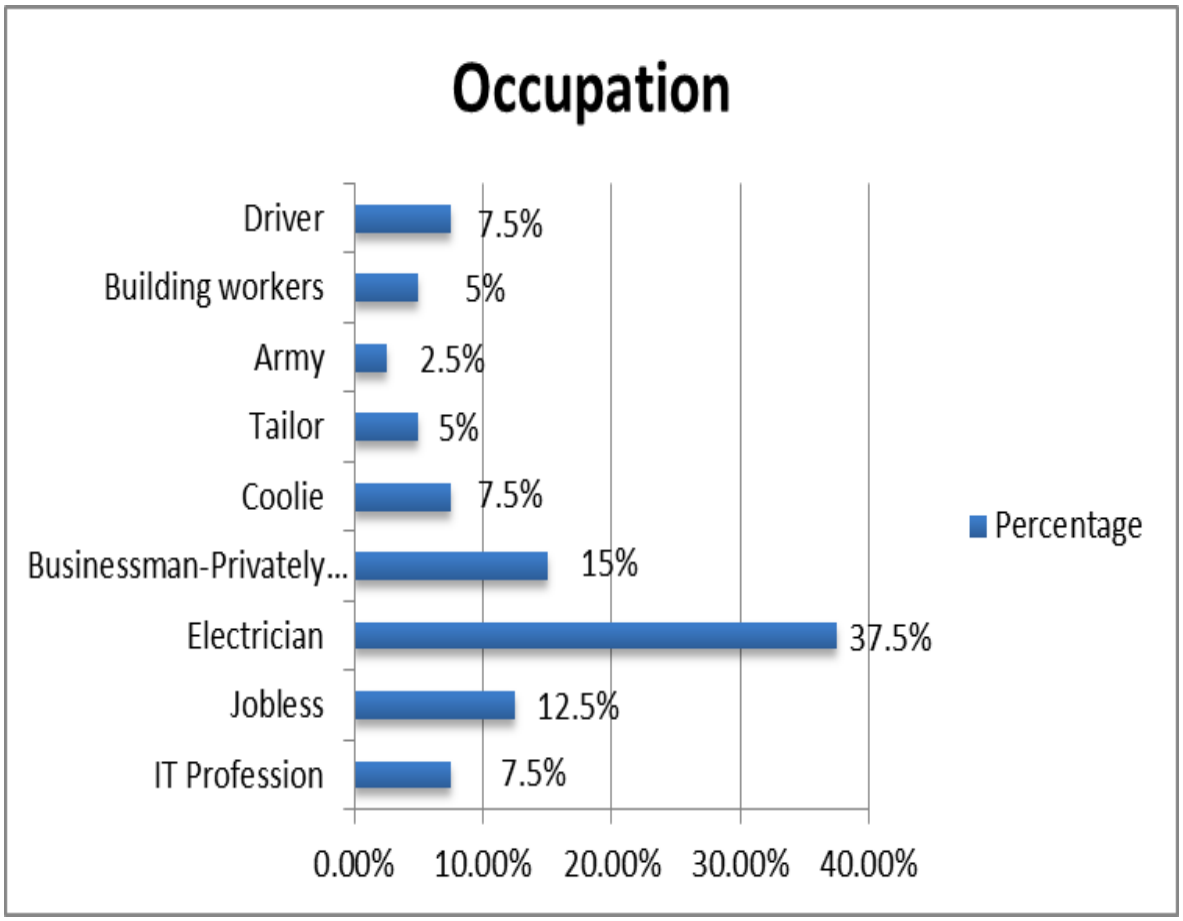


Table-3 Food habits

Sl. No	Dietary Habits	No of Cases	Percentage
1	Vegetarian	4	10%
2	Non Vegetarian	36	90%

Chart-3

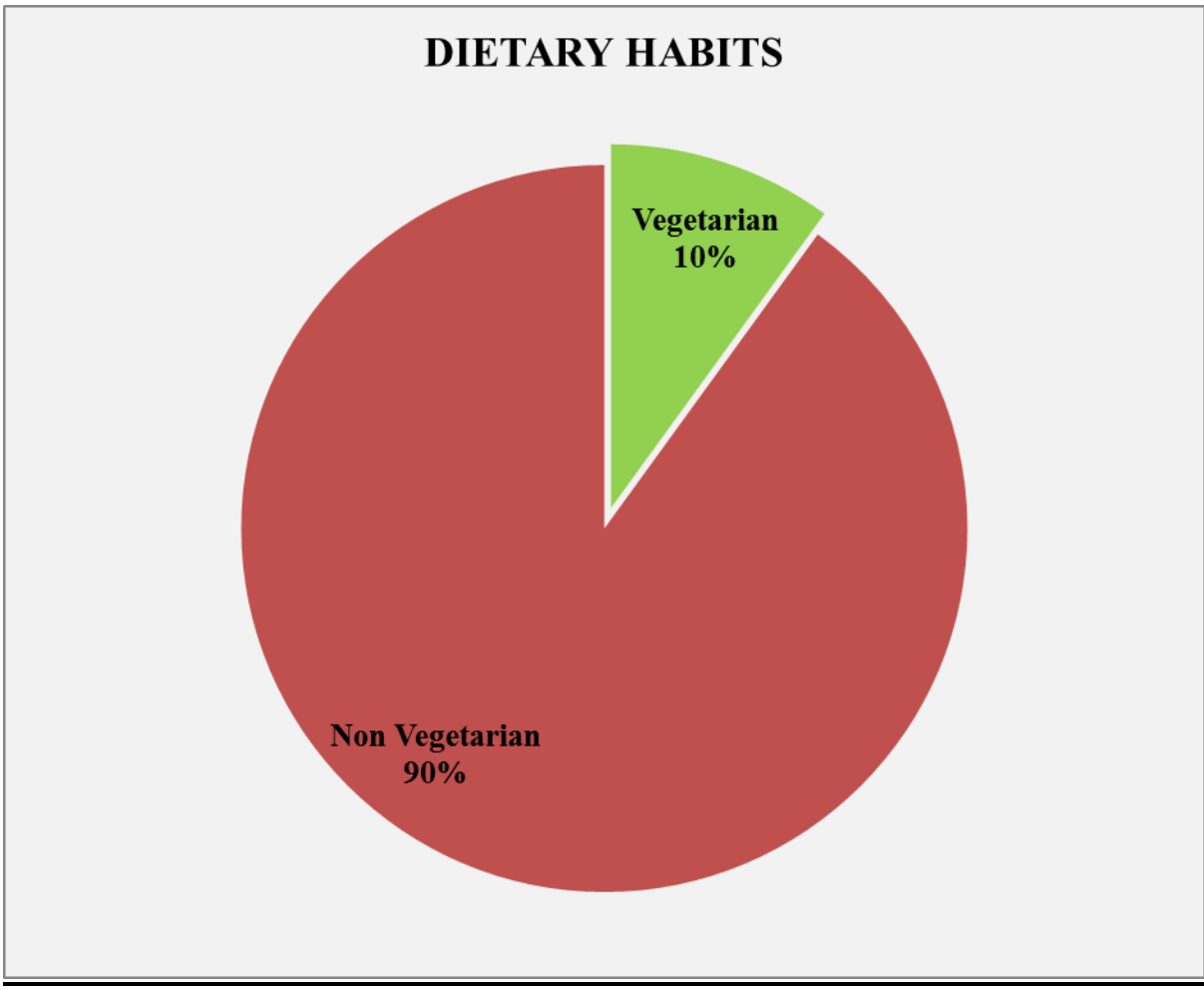


Table 4 Personal habits

Personal habits	Cases	
Smoking/alcohol/tobacco/chewing	Numbers	Percentage (%)
Smoking with alcohol	15	37.5%
Smoking	10	25%
Tobacco chewers	0	0%
None of the above habits	15	37.5%
Total	40	100%

Chart-4:

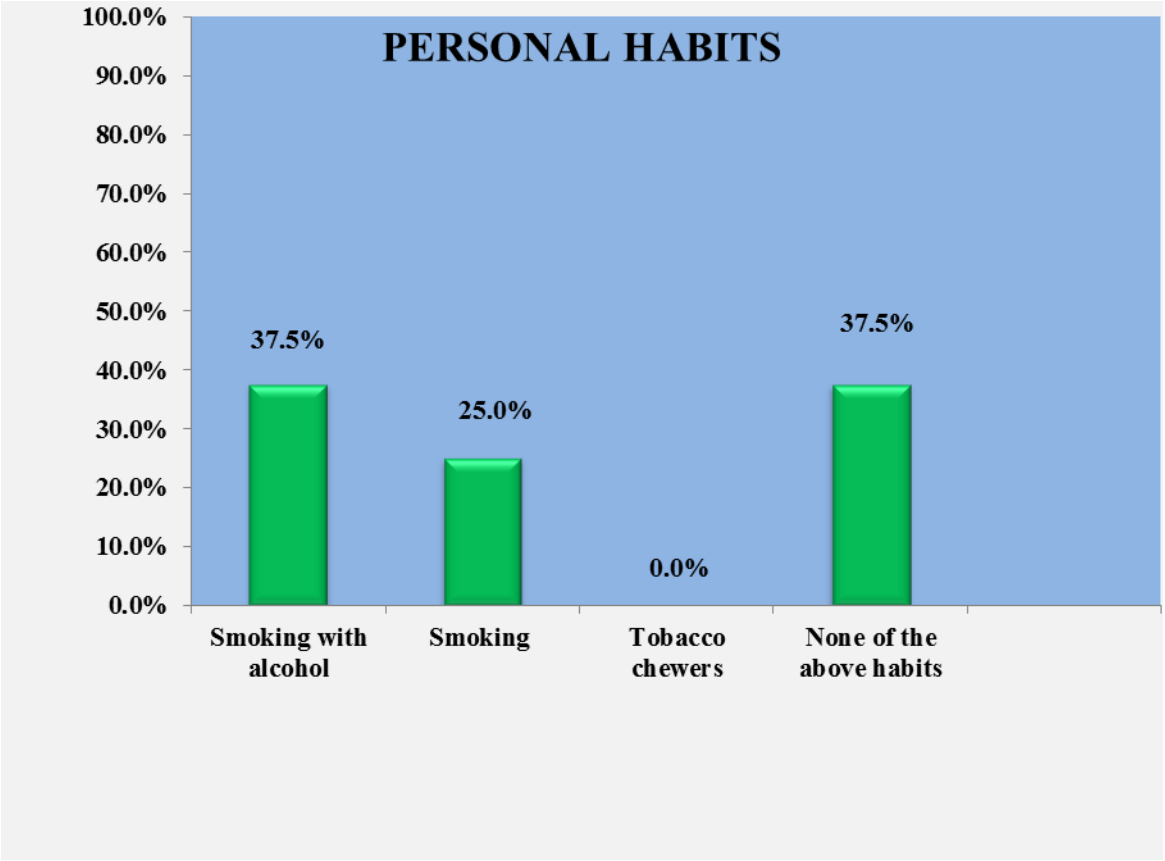


Table-5 Duration of Male Infertility

Duration (years)	Cases	
	Numbers	Percentage (%)
0 – 3	20	50
4 -6	10	25
7- 9	8	20
More than 10	2	5
Total	40	100

Chart-5:

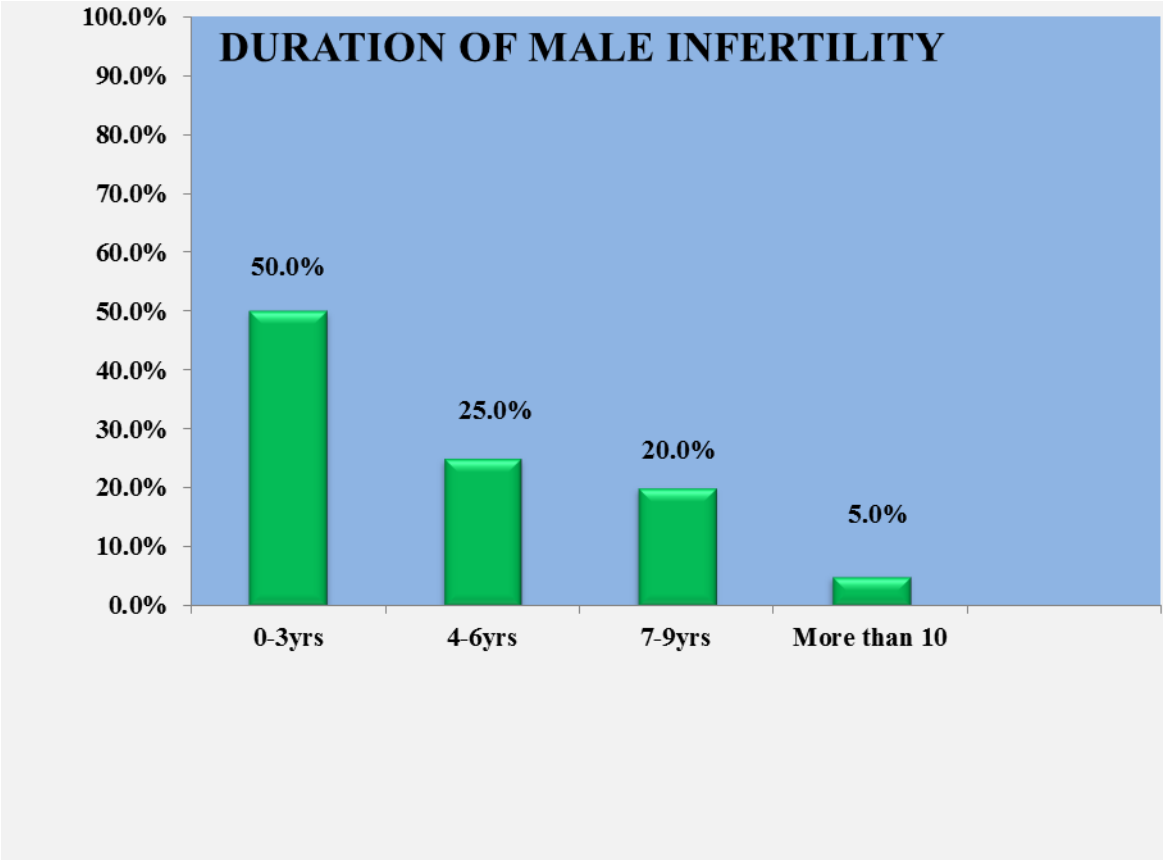


Table-6 THINAI

Thinai	cases	
	No	Percentage (%)
Kurunji	0	0
Mullai	2	5
Marutham	8	20
Neithal	30	75
Palai	0	0
Total	40	100

Chart-6:

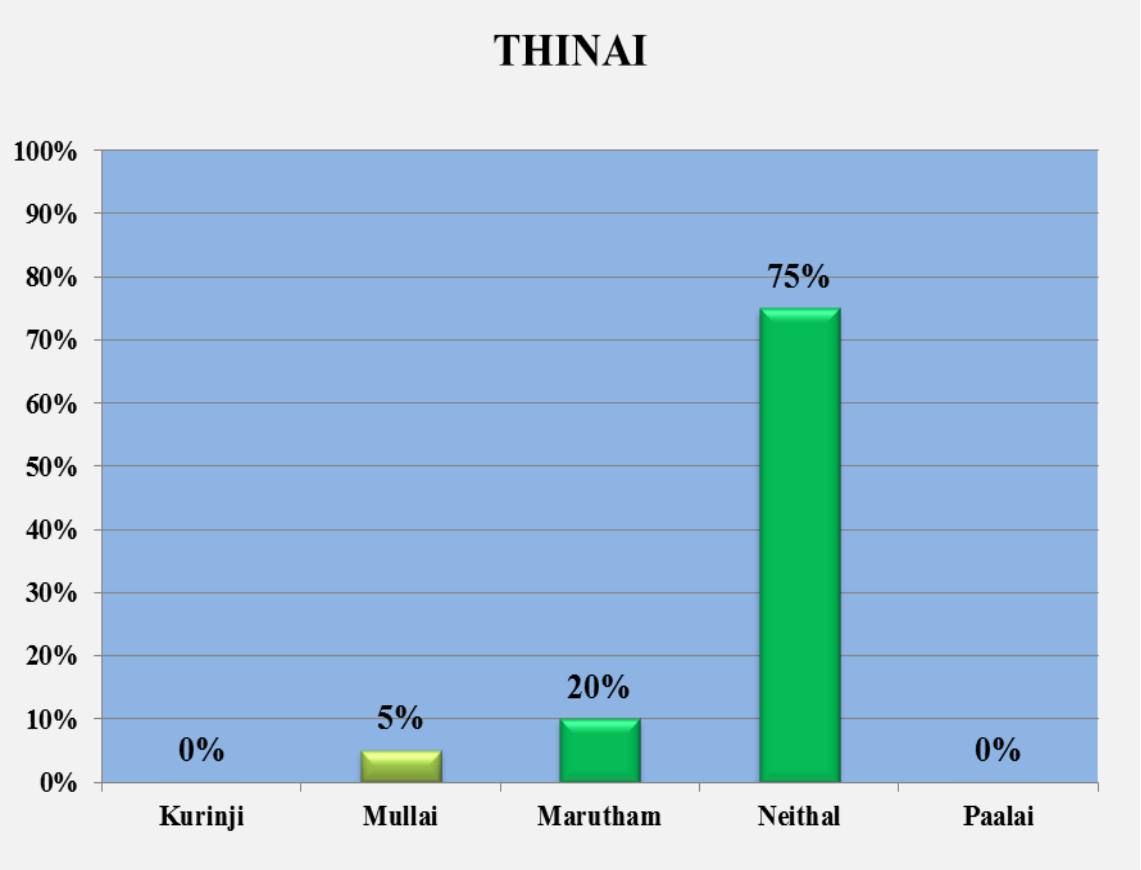


Table 7 Paruvakalam

Paruvakalam	Cases	
	No	Percentage(%)
Karkalam	0	0
Koothirkalam	0	0
(Jan-Feb)Munpanikalam	40	100%
Pinpanikalam	0	0
Elavenilkalam	0	0
Muthuvenilkalam	0	0
Total	40	100

Chart-7:

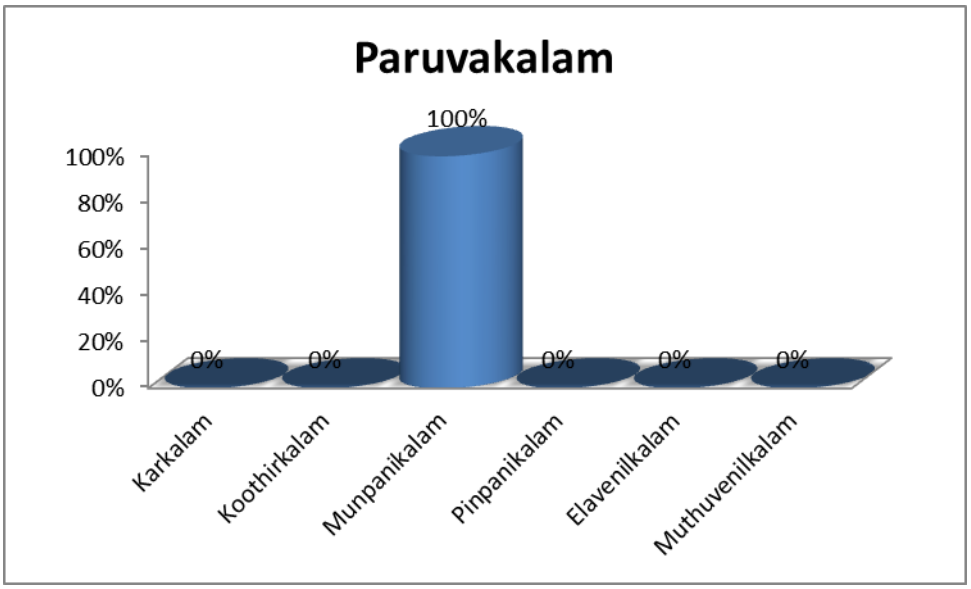


Table 8 Thegi

Type of Theygi	No of cases	Percentage
Vatha thegi	10	25
Pitha thegi	20	50
Kaba thegi	10	25

Chart-8:

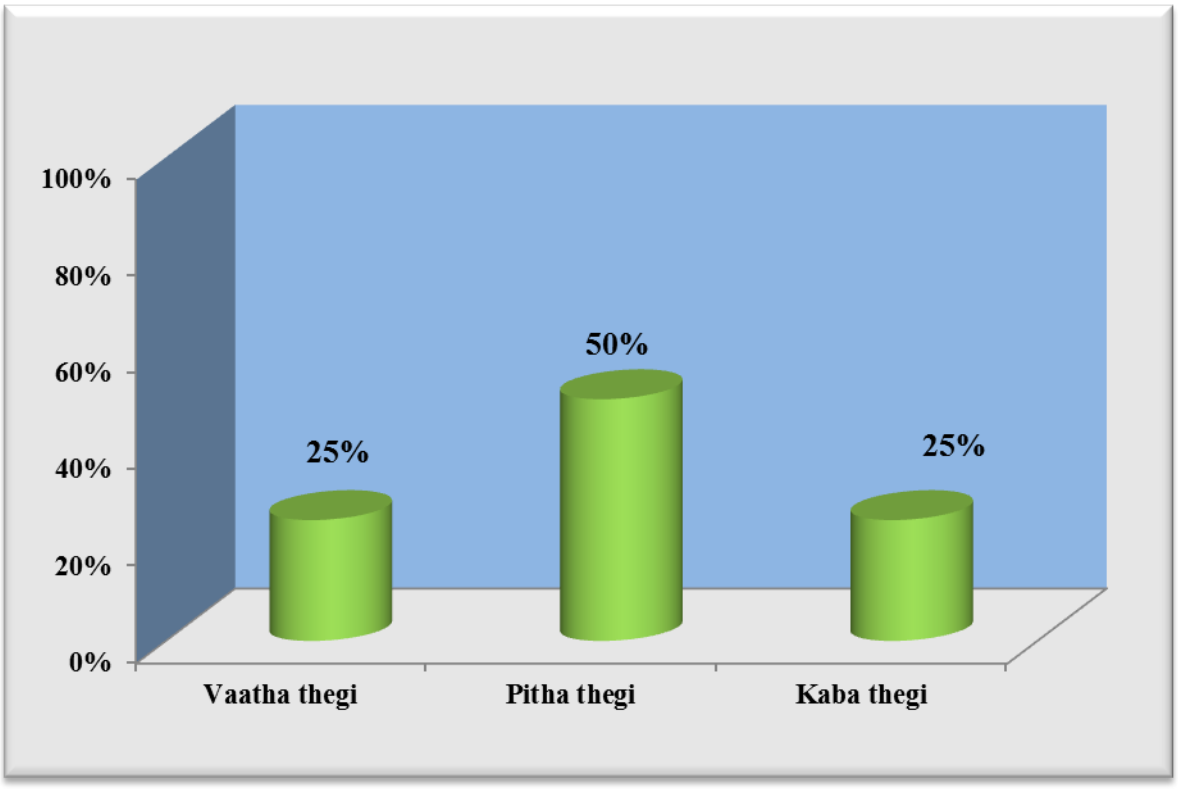
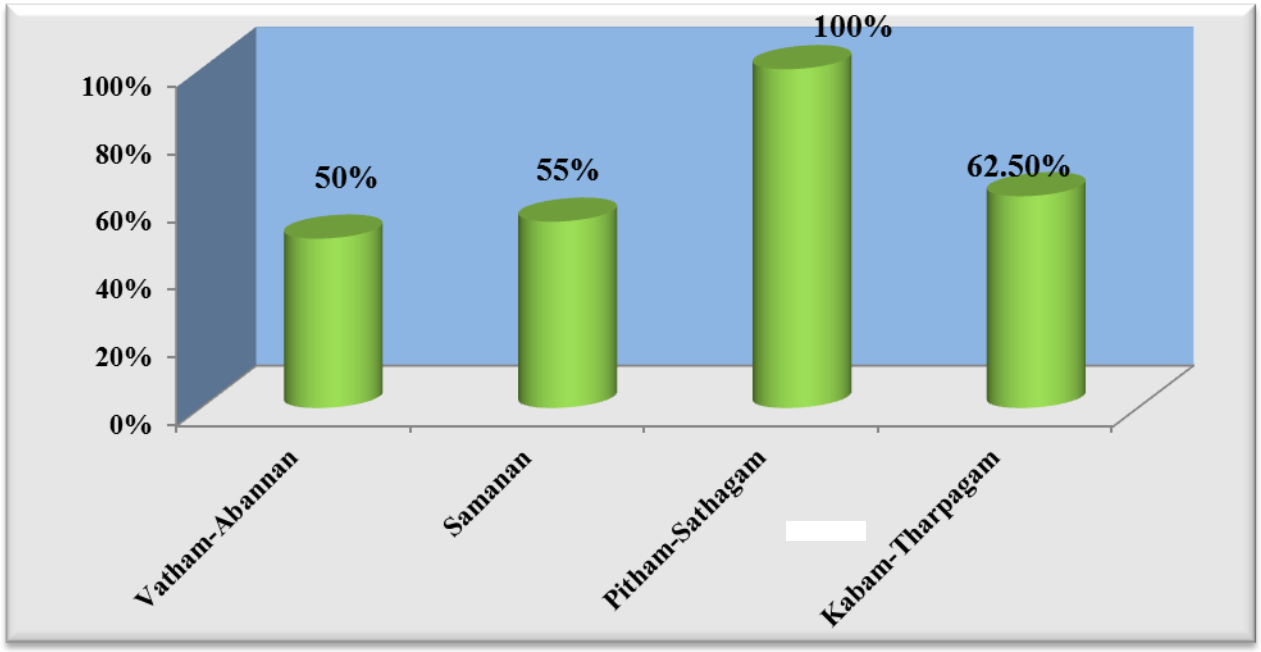


Table 9 Three Humors

Type of Humor	No of cases	Perceentage
Vatham Abannan affected in	20	50
Samanan affected in	22	55
Pitham Sathagam affected in	40	100
Kabam -Tharpagam affected in	25	62.5

Chart-9:



10 KOSAM (Five sheaths)

Type of Kosam	No of cases	Perceentage
Annamaya Kosam	40	100
Pranamaya Kosam	0	0
Manomaya Kosam	32	80
Vingnanamaya Kosam	0	0
Anandhamaya Kosam	40	100

Chart-10:

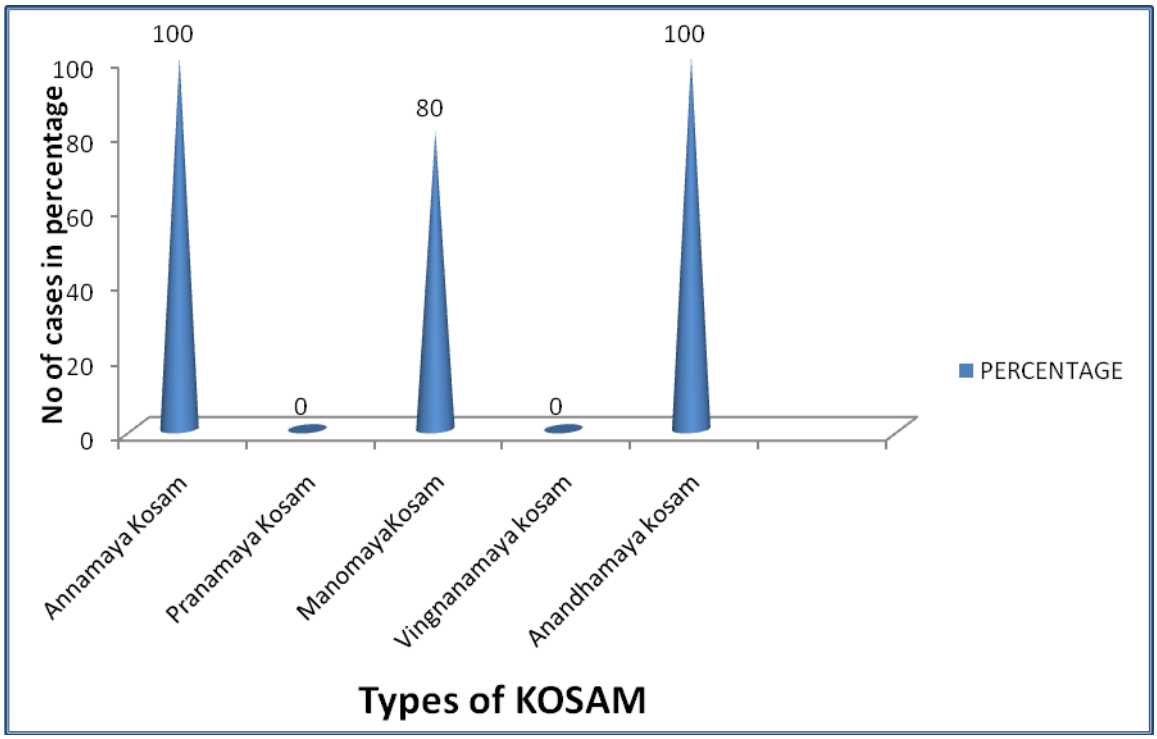


Table 11 Udal Thathukal

Udal Thathukal	Cases	
	No	Percentage (%)
Saaram	40	100
Senneer	40	100
Oon	0	0
Kozhuppu	0	0
Enbu	0	0
Moolai	0	0
Sukkilam	40	100

Chart-11:

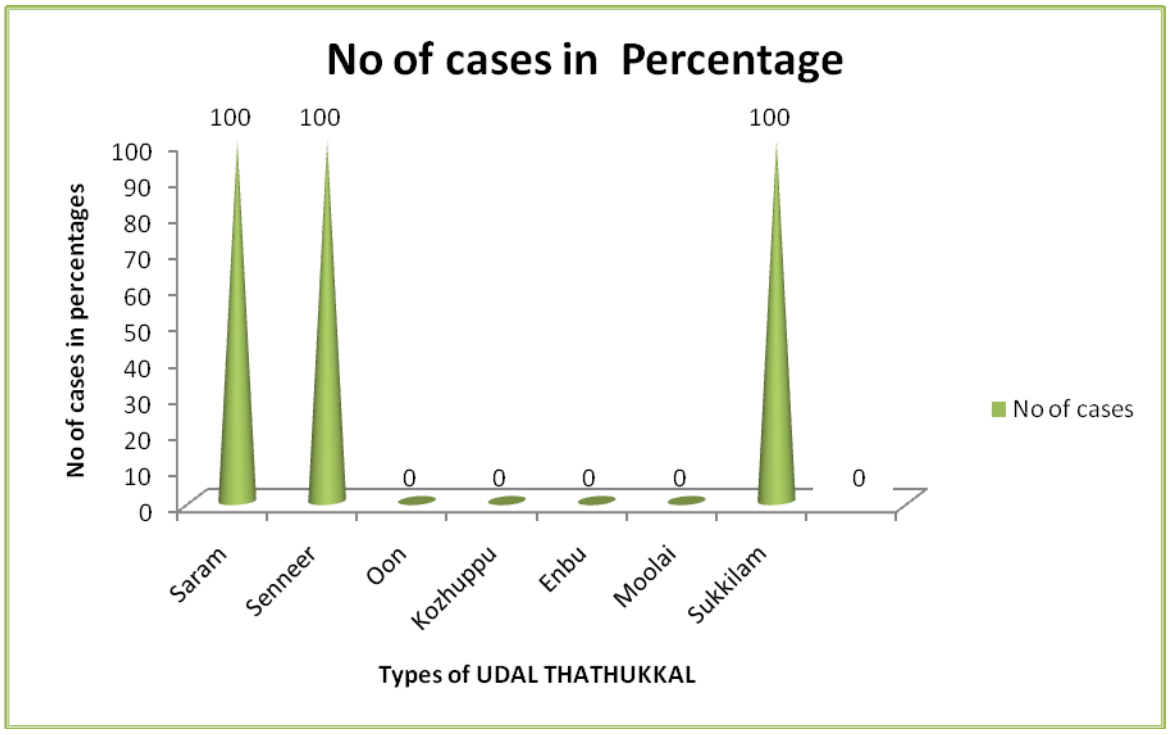
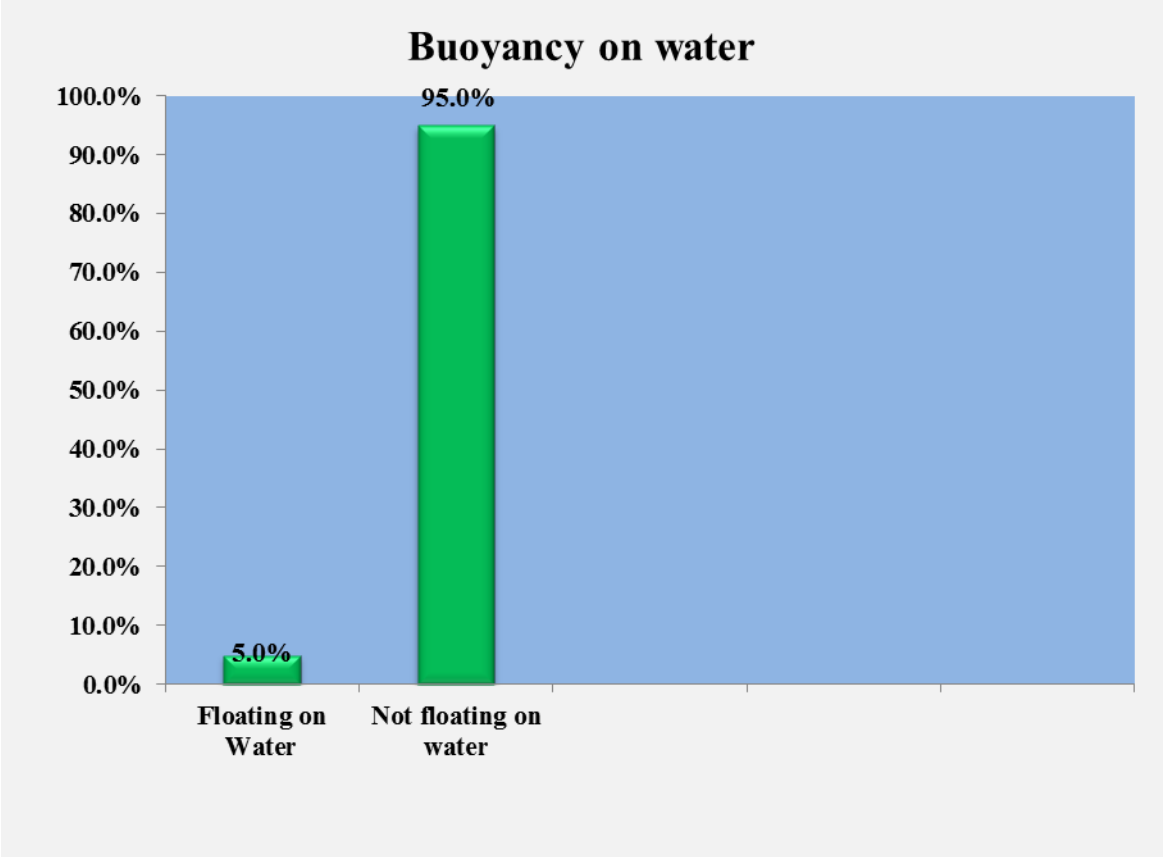


Table 12 Buoyancy on water

Buoyancy on water	No cases	Percentage (%)
Floating on Water	2	5
Not floating on Water	38	95
Total	40	100

Chart-13:



14. Neerkuri

Neerkuri	Cases	
	No	Percentage
Pale yellow	12	30
Yellow	4	10
Dark yellow	4	10
Straw	20	50
Total	40	100

Chart-14:

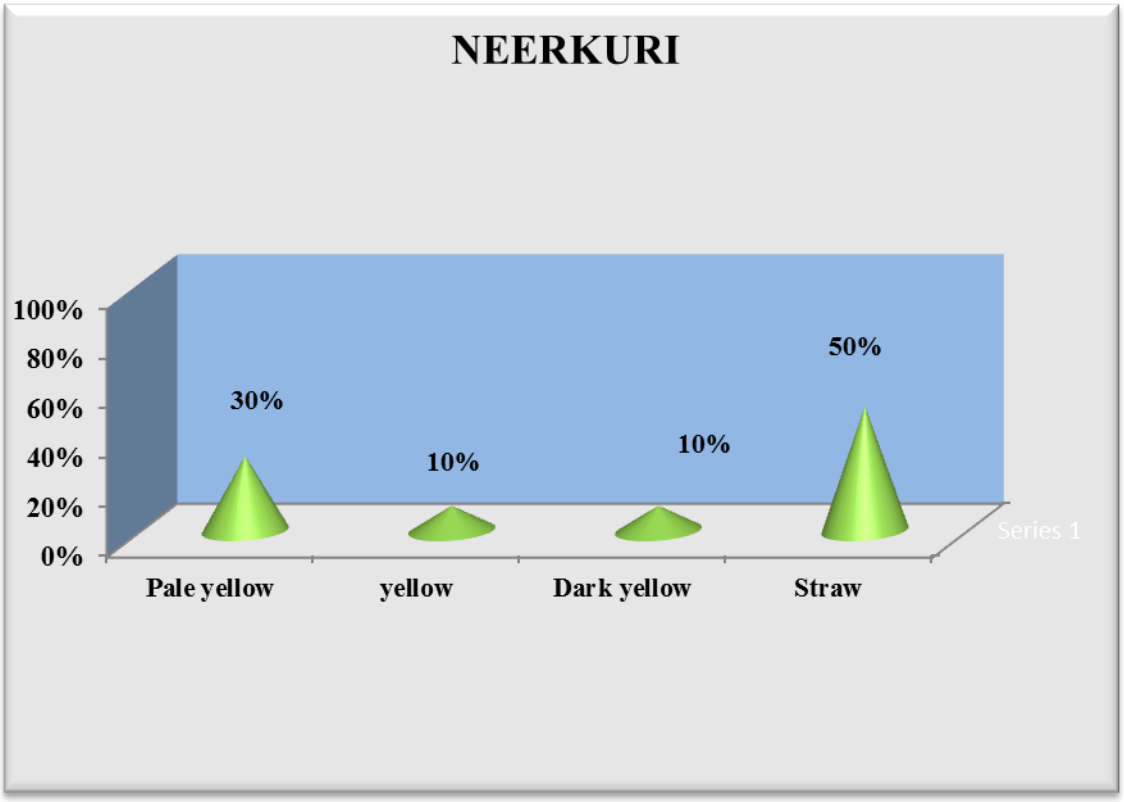


Table 15 Neikuri

Neeikuri	Cases	
	Numbers	Percentage
Slowly spread	4	10
Fastly spread	30	75
No spread	6	15
Total	40	100

Chart-15:

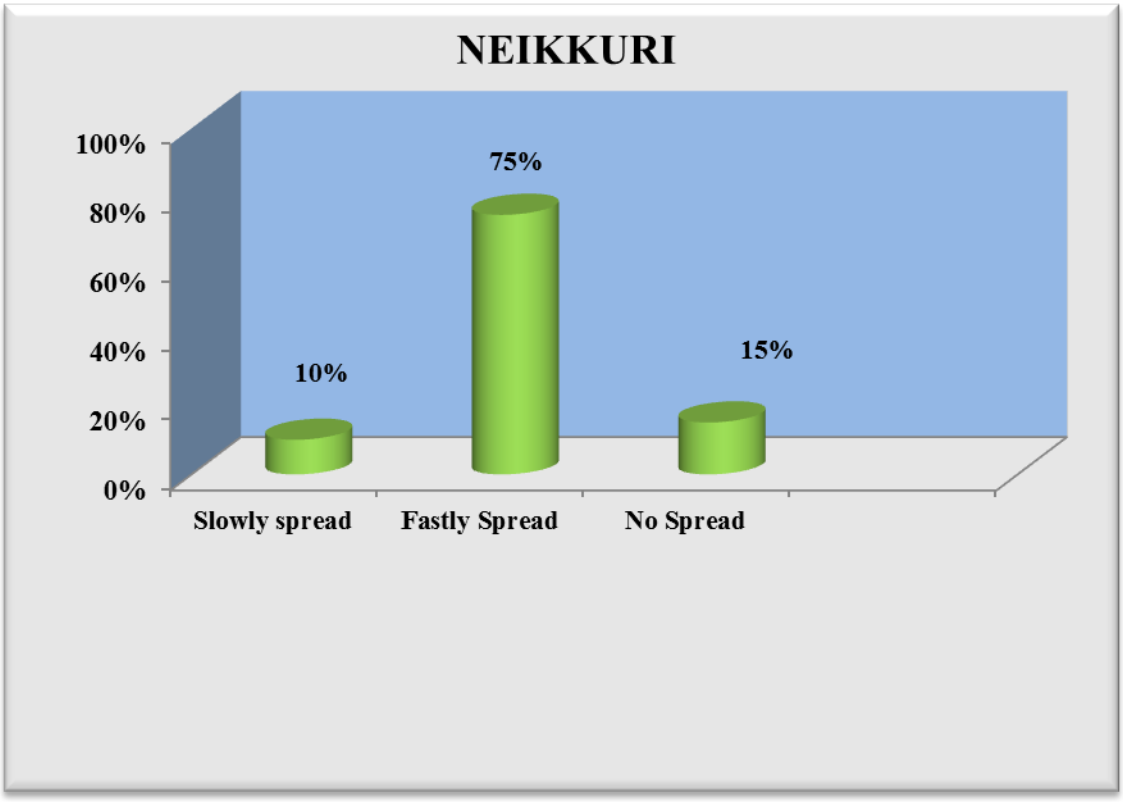


Table 16 History of Masturbation

Duration (years)	Cases	
	No	Percentage (%)
0 – 5	30	75
5 – 10	10	25
Total	40	100

Chart-16:

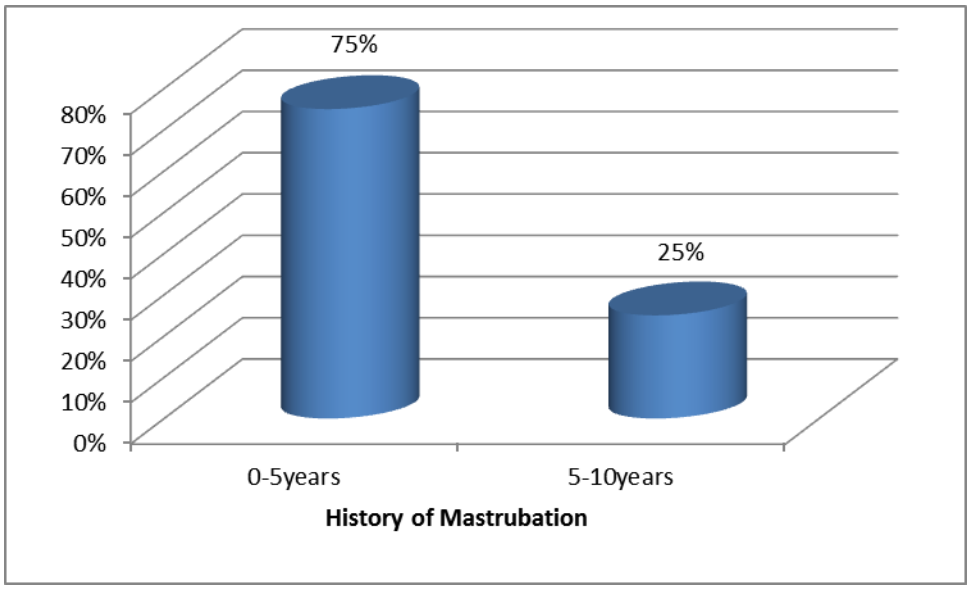


Table 17 Clinical Features

Symptoms	No of cases	Before treatment Percentage (%)	After treatment Percentage (%)
Premature ejaculation	30	75	5
Erectile dysfunction	35	87.5	7.5
Painful coitus	0	0	0
Painful Micturition	5	12.5	5
Nocturnal emission	10	25	5
Scrotal swelling	0	0	0

Chart-17:

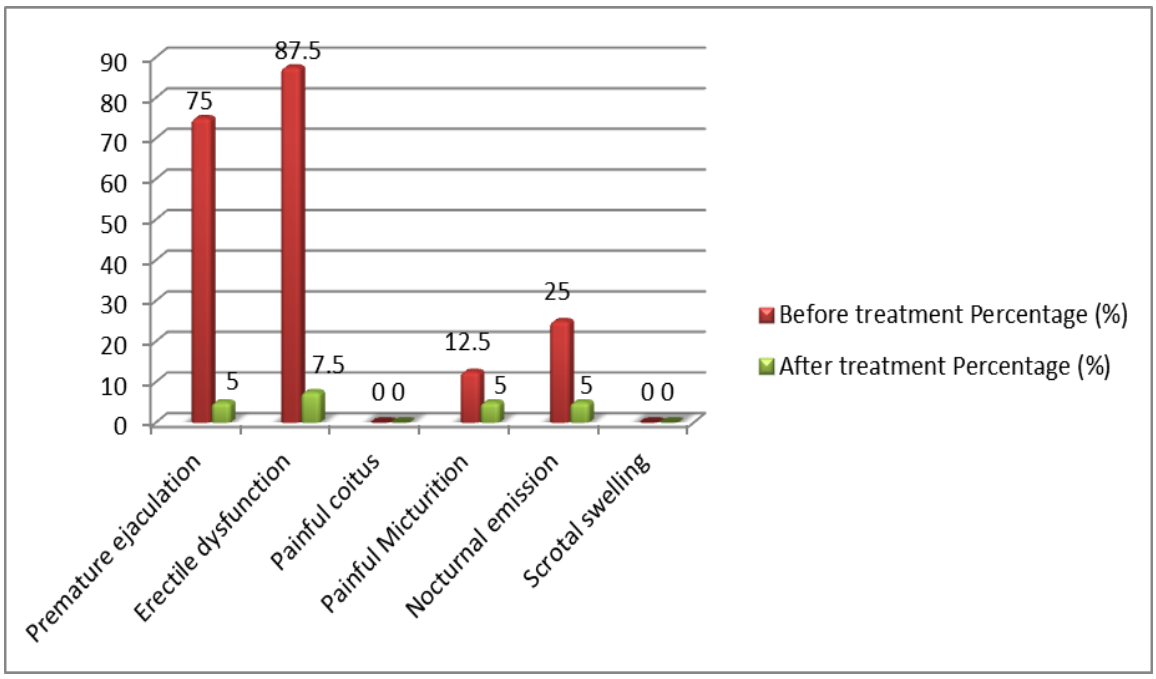


Table 18 Semen analysis- Semen Count improvement profile

Semen Count Before treatment presenting with	No of cases	%	Semen Count After treatment improved	No of cases	%
Less than 5 Million/ml	10	25	Less than 5 Million/ml	2	5
More than 5Million - 10Million/ml	8	20	More than 5Million - 10Million/ml	2	5
More than 11Million-20Million/ml	10	25	More than 11Million-20Million/ml	4	10
More than 21Million-30Million/ ml	8	20	More than 21Million-30Million/ ml	8	20
More than 30 Million/ml	4	10	More than 30 Million/ml	24	60

Chart-18:

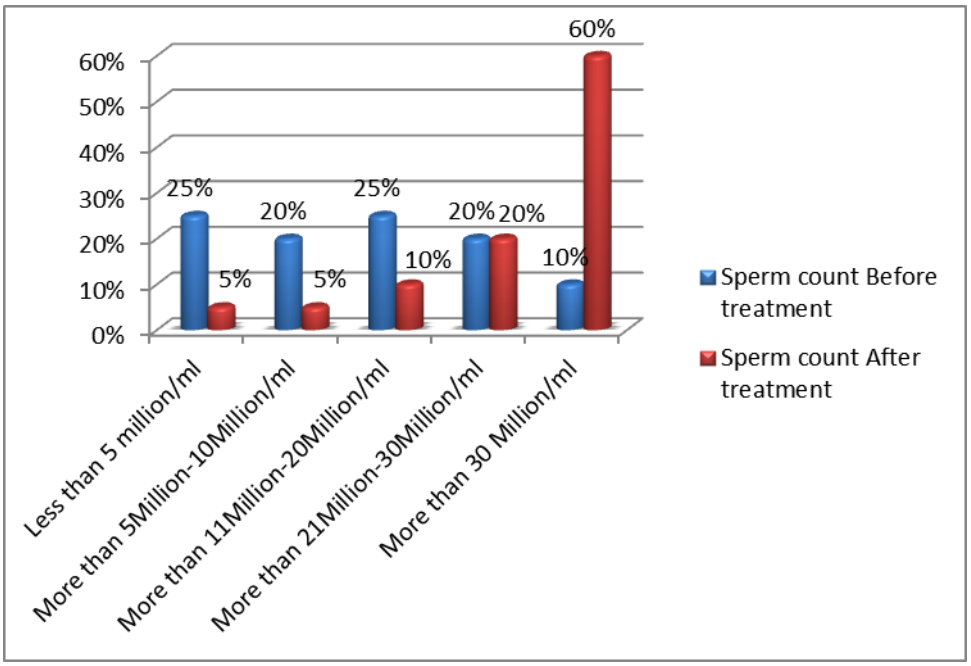
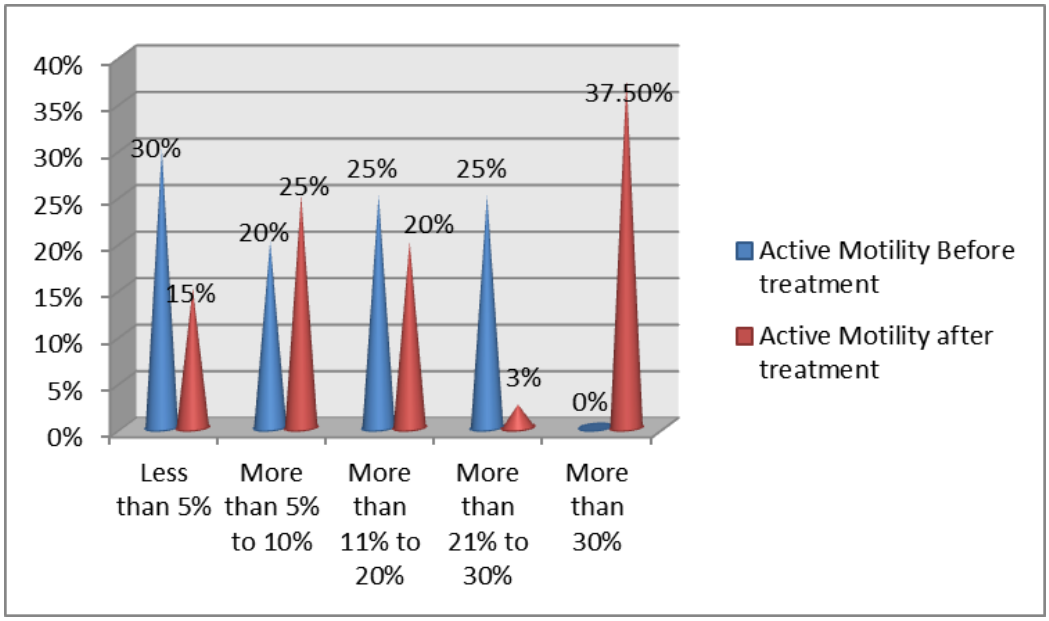


Table 19 Semen analysis - Active Motility improvement profile

Active Motility Before treatment presenting with	No of cases	%	Active Motility After treatment improved by	No of cases	%
Less than 5 %	12	30	Less than 5 %	6	15
More than 5% to 10%	8	20	More than 5% to 10%	10	25
More than 11% to 20%	10	25	More than 11% to 20%	8	20
More than 21% to 30%	10	25	More than 21% to 30%	1	2.5
More than 30 %	0	0	More than 30 %	15	37.5

Chart-19:



20. PRIMARY OUT COME

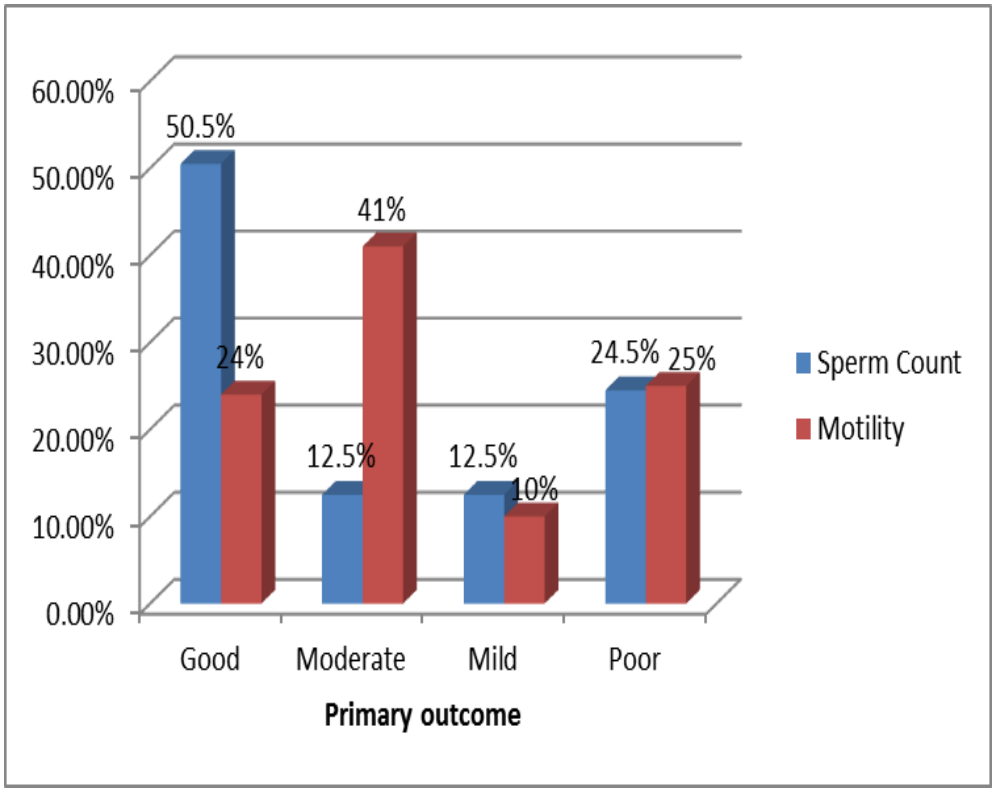
RESULT	SPERM COUNT *		No of cases	%	MOTILITY % #		No of cases	%
	FROM	TO			FROM	To		
GOOD	≤ 40 million / ejaculates	≥ 60 million / ejaculates	20	50.5	≤ 50%	≥ 70 %	10	24
MODERATE	≤ 40 million / ejaculates	> 50 million / ejaculates	6	12.5	≤ 50%	≥ 60 %	16	41
MILD	≤ 40 million / ejaculates	50 million / ejaculates	4	12.5	≤ 50%	> 50 %	4	10
POOR	1 million / ejaculates	≤ 40 million / ejaculates	10	24.5	≤ 50%	≤ 50%	10	25

Reference:

***** As per 1999 WHO criteria (1) standard value for total number of spermatozoa ≥ 40 million per ejaculates.

As per 1999 WHO criteria (1) standard value for motility is ≥ 50 % million per ejaculates.

Chart-20:


60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
50.5%
24%
12.5%
41%
12.5%
10%
24.5%
25%
Good
Moderate
Mild
Poor
Primary outcome
Sperm Count
Motility

STATISTICAL ANALYSIS

All collected data were entered into MS Excel software using different columns as variables and rows as patients. STATA software was used to perform statistical analysis. Basic descriptive statistics include frequency distributions and cross-tabulations were performed. Bar diagram are used to describe the value of different variables for pictorial representation. The quantity variables were expressed as mean standard deviation and qualitative data as percentage. A probability value of <0.05 was considered to include as statistical significance. Paired t test was performed for determining the significance between and after treatment.

Results of statistical analysis of objective parameters (semen analysis) before and after treatment of 40 patients of Aan maladu.

Sno	Parameter	Mean		Probability value(p)	t value
		BT	AT		
1	Sperm count	21.01	60.6	<1.0000	7.49
2	Sperm motility	23.25	36.75	<1.0000	5.04

Results of statistical analysis of subjective parameters before and after treatment of 40 patients of Aan maladu.

The mean $\pm$ Standard deviation of sperm count before and after treatment were 21.01 and 60.6 respectively which is statistically significant (t=7.49 P<1.0000.

The mean $\pm$ Standard deviation of sperm motility before and after treatment were 23.25 and 36.75 respectively which is statistically significant (t=5.04 P<1.0000.

LABORATORY INVESTIGATIONS

BLOOD INVESTIGATION

SL.NO	OP NO	Study No	Hb gm /dl		TRBC Million/cumm	
			Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	1	14.8	13.8	4.8	4.1
2	I 42957	2	16.6	16.4	5.6	5.4
3	G 95889	3	16.9	15.9	5.7	5.5
4	I 13253	4	17.8	15.9	6.1	5.1
5	H 72446	5	15.5	13.4	5.1	4.4
6	I 39455	6	14.6	15.1	5.0	5.2
7	I 41903	7	17.1	17.0	5.8	5.8
8	H 80572	8	15.5	15.3	6.0	5.7
9	H 70447	9	14.2	13.6	5.4	5.2
10	I 44256	10	15.5	14.9	5.2	5.0
11	I 25653	11	15.7	14.7	5.3	5.5
12	I 44516	12	14.8	13.9	4.5	4.3
13	I 16233	13	16.1	15.2	5.9	5.4
14	I 26113	14	17.6	16.3	5.8	5.4
15	I 46152	15	16.0	15.9	5.8	5.8
16	I 22106	16	16.2	15.2	4.8	4.7
17	F 042735	17	15.6	15.5	5.3	5.3
18	I 43772	18	14.5	15.5	4.9	5.0
19	I 46949	19	15.6	16.1	5.2	5.3
20	I 08792	20	16.7	15.7	5.5	5.7
21	I 17148	21	17.1	16.0	5.5	5.1
22	I 49209	22	16.7	15.7	5.8	5.4
23	I 46480	23	15.6	14.5	6.2	6.5
24	I 47208	24	13.4	14.3	3.9	4.2
25	I 48840	25	15.5	15.1	5.3	5.1
26	I 48490	26	16.8	15.8	5.7	5.6
27	I 29302	27	15.5	15.1	5.3	5.2
28	I 46426	28	17.1	16.6	6.2	6.1
29	H 86837	29	13.9	14.4	4.4	4.5
30	I 31859	30	16.4	15.4	5.5	5.3
31	I 51222	31	15.8	14.7	5.2	5.3
32	I 47764	32	15.3	16.0	5.0	5.2
33	I 53634	33	14.5	14.0	5.2	5.0
34	I 53597	34	16.7	15.7	5.3	5.0
35	I 52874	35	16.8	15.8	5.5	5.4
36	I 46955	36	14.2	13.5	4.8	4.7
37	H 74380	37	15.3	14.2	5.0	5.2
38	I 55296	38	15.6	16.0	5.5	5.7
39	I 22884	39	17.3	18.5	6.11	6.0
40	I 53967	40	17.0	17.8	5.6	5.7

BLOOD INVESTIGATION

SL.NO	OP NO	TotalWBCcount (million/cu.mm)		DC %							
		Before Treatment	After Treatment	NEUTROPHILS%		LYMPHOCYTES%		EOSINOPHILS%		MONOCYTES%	
				Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	9200	9000	66	60	27	31	-	-	07	09
2	I 42957	5800	5600	54	53	42	43	-	-	04	04
3	G 95889	8900	8700	56	55	37	38			07	07
4	I 13253	6300	6100	50	52	46	44			04	04
5	H 72446	6200	5400	68	50	26	42			06	08
6	I 39455	8200	6400	68	59	26	35			06	06
7	I 41903	7900	8100	65	69	30	26			05	05
8	H 80572	6700	6600	60	55	32	37			08	08
9	H 70447	8200	8600	65	64	30	31			05	05
10	I 44256	7400	6300	64	60	32	36			04	04
11	I 25653	11400	10400	42	45	29	26	27	27	02	02
12	I 44516	6900	6500	70	75	25	20			05	05
13	I 16233	7700	6700	66	64	30	32			04	04
14	I 26113	5900	6000	51	50	43	44			06	06
15	I 46152	10100	10100	50	55	25	25	22	19	03	01
16	I 22106	10300	9400	59	57	32	34			09	09
17	F 042735	5300	5300	66	60	29	33			05	07
18	I 43772	6700	6800	40	42	47	45	11	11	02	02
19	I 46949	6600	7700	63	63	32	31			05	06
20	I 08792	9600	9900	69	68	27	28			04	04

BLOOD INVESTIGATION

SL.NO	OP NO	TotalWBCcount (million/cu.mm)		Differential Count							
		Before Treatment	After Treatment	NEUTROPHILS %		LYMPHOCYTES%		EOSINOPHILS%		MONOCYTES%	
				Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
21	I 17148	7000	5100	70	65	22	30			08	05
22	I 49209	7300	6300	52	53	39	38			09	09
23	I 46480	7900	8100	71	70	23	24			06	06
24	I 47208	7200	7400	57	58	29	28			12	12
25	I 48840	6100	6700	46	50	47	42			07	08
26	I 48490	5500	6500	55	50	40	45			05	05
27	I 29302	8200	7400	60	55	31	37			09	08
28	I 46426	7900	6800	60	53	36	43			04	04
29	H 86837	5800	5500	62	55	32	40			06	05
30	I 31859	9000	8900	52	50	41	43			07	07
31	I 51222	7300	7100	59	60	34	33			07	07
32	I 47764	5600	5500	73	72	23	24			04	04
33	I 53634	11600	7500	59	54	36	40			05	06
7 34	I 53597	9400	8700	56	50	30	35		01	14	14
35	I 52874	11800	11500	67	66	29	30			04	04
36	I 46955	8700	8400	74	73	22	23			04	04
37	H 74380	6900	6800	46	45	48	49			06	06
38	I 55296	6900	7100	45	47	49	45			06	08
39	I 22884	9900	8700	70	65	26	27			04	08
40	I 53967	9100	9200	60	65	34	29			06	06

ERYTHROCYTE SEDEMENTATION RATE

SL.NO	OP NO	ESR		ESR	
		mm/1/2 Hr		mm/1 Hr	
		Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	10	10	20	22
2	I 42957	2	2	4	4
3	G 95889	2	2	4	4
4	I 13253	2	2	4	4
5	H 72446	2	4	4	8
6	I 39455	4	2	8	6
7	I 41903	2	2	4	4
8	H 80572	2	2	4	4
9	H 70447	16	12	32	24
10	I 44256	2	4	4	8
11	I 25653	2	2	4	4
12	I 44516	2	2	6	4
13	I 16233	8	8	16	16
14	I 26113	2	2	4	4
15	I 46152	2	2	4	6
16	I 22106	6	6	12	12
17	F 042735	10	4	22	8
18	I 43772	8	4	16	8
19	I 46949	4	2	8	4
20	I 08792	2	2	4	4
21	I 17148	4	14	8	30
22	I 49209	2	2	4	4
23	I 46480	10	10	22	22
24	I 47208	4	4	10	10
25	I 48840	2	2	4	4
26	I 48490	2	2	4	4
27	I 29302	2	4	4	8
28	I 46426	4	4	8	8
29	H 86837	4	8	8	16
30	I 31859	4	4	8	8
31	I 51222	2	2	4	4
32	I 47764	6	7	12	14
33	I 53634	4	10	10	20
34	I 53597	4	6	8	12
35	I 52874	2	8	4	16
36	I 46955	12	8	26	16
37	H 74380	10	8	20	16
38	I 55296	2	8	4	16
39	I 22884	2	2	4	4
40	I 53967	2	2	4	4

LIPID PROFILE

SL.NO	OP NO	T.Cholesterol (mg/dl)		HDL (mg/dl)		LDL (mg/dl)		VLDL (mg/dl)		TGL (mg/dl)	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	114	109	38	28	59	63	18	36	90	140
2	I 42957	165	190	48	45	89	95	20	25	101	120
3	G 95889	149	155	43	45	87	90	41	39	203	150
4	I 13253	160	160	44	36	85	97	37	42	183	209
5	H 72446	117	131	49	38	65	75	19	39	95	198
6	I 39455	194	218	65	50	107	136	23		113	427
7	I 41903	230	177	57	38	133	113	25	55	124	273
8	H 80572	164	169	53	33	88	97	32		161	426
9	H 70447	161	176	50	42	96	106	24	33	118	167
10	I 44256	148	191	45	37	87	124	28	51	139	258
11	I 25653	171	169	43	50	96	90	41	45	203	199
12	I 44516	124	163	48	38	77	100	18	39	90	196
13	I 16233	184	194	58	56	101	110	29	39	146	140
14	I 26113	149	171	47	40	90	106	22	58	111	289
15	I 46152	104	183	33	34	67	111	15		77	502
16	I 22106	227	207	43	40	143	140	27	35	137	140
17	F 042735	153	175	55	38	86	105	15	61	77	306
18	I 43772	147	152	47	40	78	70	17	25	86	90
19	I 46949	129	142	41	36	74	84	25	43	126	218
20	I 08792	124	134	40	45	74	80	12	20	61	65

LIPID PROFILE

SL.NO	OP NO	T.Cholesterol (mg/dl)		HDL (mg/dl)		LDL (mg/dl)		VLDL (mg/dl)		TGL (mg/dl)	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
21	I 17148	161	164	43	39	97	101	19	24	97	123
22	I 49209	200	195	50	40	122	120	23	25	117	110
23	I 46480	151	160	34	38	94	90	35	38	176	165
24	I 47208	140	160	56	55	78	75	14	20	72	75
25	I 48840	149	185	42	38	89	113	20	63	102	316
26	I 48490	101	115	41	40	54	56	12	20	60	65
27	I 29302	162	179	45	36	97	110	27	56	133	280
28	I 46426	188	186	44	43	119	109	32	53	158	268
29	H 86837	92	135	32	31	53	83	11	36	55	181
30	I 31859	174	136	54	39	104	77	22	43	112	215
31	I 51222	131	135	47	48	74	70	30	35	147	160
32	I 47764	147	150	65	60	85	84	08	20	38	140
33	I 53634	160	165	57	40	99	103	28	49	139	247
34	I 53597	148	167	38	23	88	101	45	40	224	200
35	I 52874	213	200	60	55	128	125	26	35	129	130
36	I 46955	188	190	40	45	82	89	72	70	359	300
37	H 74380	205	201	43	46	121	125	36	35	181	180
38	I 55296	190	195	40	45	120	125	35	40	150	155
39	I 22884	196	116	37	37	50	73	37	53	186	268
40	I 53967	138	145	39	45	81	90	30	35	150	155

LIVER FUNCTION TEST **BLOOD SUGAR PROFILE**

SL.NO	OP NO	Serum Bilirubin (mg/dl)						Glucose Profile mg/dl					
		Direct		Indirect		Total		Fasting		Post prandial		Random	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	0.8	0.2	1.6	1.0	2.4	1.2	69	100	71	140		
2	I 42957	0.2	0.2	0.4	0.6	0.6	0.8	80	90	119	130		
3	G 95889	0.3	0.3	0.4	0.5	0.7	0.8					62	110
4	I 13253	0.4	0.4	0.6	0.7	1.0	1.1	63	101	67	108		
5	H 72446	0.3	0.3	0.4	0.4	0.7	0.7	80		90			107
6	I 39455	0.4	0.4	0.4	0.8	0.8	1.2	79	124	140	127		
7	I 41903	0.5	0.7	1.3	2.0	1.8	2.7	68	96	86	139		
8	H 80572	0.2	0.2	0.3	0.5	0.5	0.7					79	95
9	H 70447	0.3	0.3	0.4	0.4	0.7	0.7	72	108	129	155		
10	I 44256	0.2	0.3	0.3	0.7	0.5	1.0					76	97
11	I 25653	0.2	0.2	0.3	0.5	0.5	0.7					74	87
12	I 44516	0.5	0.6	0.7	1.3	1.2	1.9	81	95	116	119		
13	I 16233	0.3	0.3	0.3	0.7	0.6	1.0	83	93	112	120		
14	I 26113	0.5	0.6	0.9	1.2	1.4	1.8	80	110	60	111		
15	I 46152	0.3	0.5	0.5	1.0	0.8	1.5					84	123
16	I 22106	0.4	0.3	1.0	0.7	1.4	1.0					58	110
17	F 042735	0.3	0.3	0.4	0.6	0.7	0.9	76	104	88	115		
18	I 43772	0.3	0.3	0.2	0.5	0.5	0.8					89	100
19	I 46949	0.3	0.7	0.7	0.5	1.0	1.2		110		111	78	

LIVER FUNCTION TEST **BLOOD SUGAR PROFILE**

SL.NO	OP NO	Serum Bilirubin (mg/dl)						Glucose Profile mg/dl					
		Direct		Indirect		Total		Fasting		Post prandial		Random	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
20	I 08792	0.3	0.3	0.7	0.5	1.0	0.8	72	83	84	95		
21	I 17148	0.1	0.4	0.3	0.7	0.4	1.1					71	110
22	I 49209	0.2	0.3	0.4	0.5	0.6	0.8	70	90	92	110		
23	I 46480	0.3	0.2	0.5	0.6	0.8	0.8					101	110
24	I 47208	0.3	0.3	0.4	0.5	0.7	0.8	70	80	129	125		
25	I 48840	0.3	0.2	0.4	0.5	0.7	0.7	80	109	75	140		
26	I 48490	0.6	0.4	0.8	0.7	1.4	1.1					77	87
27	I 29302	0.3	0.4	0.6	0.8	0.9	1.2	84					104
28	I 46426	0.5	0.4	1.2	0.7	1.7	1.1	69		113			123
29	H 86837	0.6	0.4	0.9	0.8	1.5	1.2	60	95	69	110		
30	I 31859	0.2	0.4	0.3	0.5	0.5	0.9					69	129
31	I 51222	0.4	0.4	0.9	0.8	1.3	1.2	69	75	58	110		
32	I 47764	0.8	0.8	1.2	0.4	2.0	1.2					69	75
33	I 53634	0.2	0.2	0.2	0.3	0.4	0.5		117		189	78	
34	I 53597	0.3	0.5	0.8	1.1	1.1	1.6					76	93
35	I 52874	0.2	0.3	0.5	0.6	0.7	0.9	63	70	71	90		
36	I 46955	0.3	0.3	0.3	0.5	0.6	0.8					126	130
37	H 74380	0.3	0.3	0.5	0.7	0.8	1.0	108	100	111	120		
38	I 55296	0.3	0.3	0.6	0.7	0.9	1.0	105	100	120	125		
39	I 22884	0.4	0.4	0.4	0.7	0.8	1.1					91	160
40	I 53967	0.3	0.3	0.4	0.5	0.7	0.8	106	90	107	110		

LIVER FUNCTION TEST

SL. NO	OP NO	SGOT (IU/L)		SGPT (IU/L)		serumAlkaline phosphatase (IU/L)		SerumAlbumin (gms/dl)		SerumGlobulin (gms/dl)		SerumTotal Protein (gms/dl)	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	27	40	28	86	65	56	4.7	4.6	3.3	3.2	8.0	7.8
2	I 42957	34	30	55	50	78	80	4.9	4.5	2.7	2.9	7.6	7.4
3	G 95889	25	20	33	30	69	60	4.7	4.2	3.1	3.2	7.8	7.4
4	I 13253	18	24	16	47	86	87	4.7	4.5	2.6	2.5	7.3	7.0
5	H 72446	19	51	14	132	60	43	4.6	4.6	3.0	2.6	7.5	7.2
6	I 39455	21	31	19	60	100	93	4.6	4.7	3.0	2.7	7.6	7.4
7	I 41903	23	82	27	187	61	70	4.5	4.3	2.6	2.9	7.1	7.2
8	H 80572	13	61	15	182	46	44	4.6	4.4	3.1	3.0	7.7	7.4
9	H 70447	49	35	71	69	94	91	4.4	4.5	3.5	3.4	7.9	7.9
10	I 44256	26	143	47	462	92	72	4.7	4.6	2.9	2.9	7.6	7.5
11	I 25653	20	30	19	29	87	80	4.5	4.4	3.0	3.0	7.5	7.4
12	I 44516	17	14	16	307	40	42	4.3	4.4	3.1	3.0	7.4	7.4
13	I 16233	20	30	21	20	81	80	4.0	4.0	3.0	3.4	7.0	7.4
14	I 26113	26	50	51	146	79	64	4.9	4.7	2.5	2.4	7.4	7.1
15	I 46152	19	63	22	129	54	60	7.4	4.8	3.3	3.4	7.7	8.2
16	I 22106	22	23	26	30	97	90	4.2	4.0	3.0	3.4	7.2	7.4
17	F 042735	24	29	20	34	76	70	4.2	4.4	2.6	3.3	6.9	7.0
18	I 43772	18	20	11	35	79	90	4.5	4.0	3.7	3.4	8.2	7.4
19	I 46949	18	46	18	129	61	44	4.2	4.5	2.4	2.6	6.6	7.0
20	I 08792	16	18	19	25	40	60	4.7	4.7	2.7	2.7	7.4	7.4

LIVER FUNCTION TEST

SL.NO	OP NO	SGOT (IU/L)		SGPT (IU/L)		serumAlkaline phosphatase (IU/L)		SerumAlbumin (gms/dl)		SerumGlobulin (gms/dl)		SerumTotal Protein (gms/dl)	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
21	I 17148	20	22	20	35.4	80	65	4.5	4.8	3.0	2.8	7.5	7.6
22	I 49209	21	20	34	40	78	81	4.6	4.0	2.9	3.4	7.5	7.4
23	I 46480	14	15	21	25	59	60	4.4	4.2	3.0	3.2	7.4	7.2
24	I 47208	20	25	20	40	79	85	4.7	4.8	3.6	3.5	8.3	8.3
25	I 48840	23	19	29	35	106	88	4.4	4.5	2.7	2.6	7.1	7.1
26	I 48490	21	25	35	36	54	60	4.7	4.0	2.5	3.0	7.2	7.4
27	I 29302	23	69	36	131	76	65	4.4	4.5	2.6	2.5	7.0	7.1
28	I 46426	18	12	19	25	71	53	4.3	4.6	3.5	3.0	7.8	7.6
29	H 86837	18	84	22	308	82	92	4.5	4.5	2.5	2.7	7.0	7.2
30	I 31859	18	25	32	50	50	38	4.3	4.3	3.3	3.1	7.6	7.4
31	I 51222	30	35	28	25	74	70	4.5	4.0	3.5	3.4	8.0	7.4
32	I 47764	19	20	07	25	84	80	4.7	4.7	2.7	2.7	7.4	7.4
33	I 53634	21	34	23	60	87	83	4.7	4.0	3.4	3.4	8.1	7.4
34	I 53597	17	87	23	26	65	60	4.6	4.4	2.9	2.7	7.5	7.1
35	I 52874	20	21	38	30	101	90	4.4	4.3	3.6	3.7	8.0	8.0
36	I 46955	20	25	33	30	85	80	4.3	4.0	2.8	3.3	7.1	7.3
37	H 74380	20	15	27	30	59	65	4.4	3.5	3.2	4.0	7.6	7.5
38	I 55296	20	25	35	36	40	50	4.0	4.0	3.4	3.2	7.4	7.2
39	I 22884	15	41	37	96	82	83	4.5	4.6	2.7	2.6	7.2	7.2
40	I 53967	24	30	31	25	87	90	4.4	4.2	2.9	2.5	7.3	7.2

RENAL FUNCTION TEST

SL. NO	OP NO	UREA mg/dl		CREATININE mg/dl		URIC ACID mg/dl	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	16	15	0.9	1.0	6.6	7.9
2	I 42957	20	25	0.9	1.1	5.7	6.0
3	G 95889	14	18	1.0	1.1	4.6	4.4
4	I 13253	19	18	0.9	0.9	5.7	6.7
5	H 72446	18	18	1.0	1.0	5.5	7.3
6	I 39455	12	12	0.9	1.0	5.1	6.0
7	I 41903	12	14	0.9	1.0	6.1	6.5
8	H 80572	18	15	0.9	0.9	4.0	5.2
9	H 70447	18	15	0.9	0.9	7.4	7.4
10	I 44256	28	21	0.9	0.7	4.8	5.7
11	I 25653	15	17	0.9	1.0	6.1	6.5
12	I 44516	16	20	1.0	1.0	4.6	4.8
13	I 16233	18	19	0.9	1.0	4.5	4.7
14	I 26113	13	14	1.2	1.2	5.2	5.9
15	I 46152	33	19	0.9	1.0	5.0	6.2
16	I 22106	17	18	1.0	1.0	6.4	7.4
17	F 042735	18	17	1.1	1.2	3.4	3.7
18	I 43772	20	25	0.9	1.0	5.4	5.5
19	I 46949	16	23	1.0	1.0	6.7	7.9
20	I 08792	17	18	1.0	1.0	6.5	6.4
21	I 17148	14	31	0.9	0.9	5.8	7.1
22	I 49209	17	19	1.2	1.2	6.9	6.5
23	I 46480	19	21	1.1	1.1	7.2	7.0
24	I 47208	10	18	0.8	0.7	2.7	2.8
25	I 48840	19	25	0.9	1.0	5.0	5.6
26	I 48490	36	37	0.9	1.0	4.7	4.5
27	I 29302	20	19	1.0	1.0	5.4	6.9
28	I 46426	18	33	1.0	1.2	6.1	6.9
29	H 86837	37	20	0.9	1.0	5.4	6.5
30	I 31859	18	16	1.1	1.2	6.7	8.0
31	I 51222	16	20	0.9	1.0	5.3	5.4
32	I 47764	31	30	0.9	1.0	3.6	3.5
33	I 53634	15	25	1.0	0.9	7.4	7.3
34	I 53597	17	23	1.2	1.11	6.1	6.8
35	I 52874	17	18	1.0	1.2	6.0	6.8
36	I 46955	13	16	0.8	0.9	7.3	7.2
37	H 74380	14	16	0.9	1.0	5.6	5.5
38	I 55296	16	20	1.0	1.2	5.5	5.4
39	I 22884	18	19	1.2	1.2	4.8	6.4
40	I 53967	17	18	1.0	1.2	6.4	6.3

SEMEN ANALYSIS

SL.NO	OP NO	Sperm Count/ml		Motility %		Morphology%	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	30	130	30	70	40	90
2	I 42957	38	50	20	50	40	60
3	G 95889	8	30	10	30	40	40
4	I 13253	14	110	10	10	40	50
5	H 72446	40	100	40	45	40	50
6	I 39455	30	35	10	10	90	90
7	I 41903	13	18	20	22	94	95
8	H 80572	3	110	10	10	50	90
9	H 70447	37.5	80	05	10	90	90
10	I 44256	4.2	19.2	30	40	40	60
11	I 25653	30	80	40	50	40	50
12	I 44516	12	20	10	15	40	50
13	I 16233	18	80	40	55	50	50
14	I 26113	1	100	40	50	50	50
15	I 46152	40	45	30	40	50	50
16	I 22106	30	60	10	10	50	50
17	F 042735	12	110	20	80	40	90
18	I 43772	20	45	40	55	90	90
19	I 46949	2.1	50	05	10	90	90
20	I 08792	33	40	30	30	90	90
21	I 17148	20	55	30	70	40	90
22	I 49209	25	90	10	15	90	90
23	I 46480	32	45	10	20	50	50
24	I 47208	39	60	30	35	40	60
25	I 48840	11	70	30	60	60	60
26	I 48490	7	15	10	10	40	40
27	I 29302	21	25	10	10	20	20
28	I 46426	8.0	62.8	20	53	30	76
29	H 86837	4	50	10	60	20	50
30	I 31859	34	120	40	50	60	60
31	I 51222	6	10	10	10	40	40
32	I 47764	14	20	20	30	40	40
33	I 53634	26	12	30	10	40	40
34	I 53597	26	32	30	10	40	40
35	I 52874	6	45	40	55	10	60
36	I 46955	30	110	30	60	78	80
37	H 74380	35	60	40	55	55	60
38	I 55296	20	60	30	60	40	60
39	I 22884	35	110	20	50	40	80
40	I 53967	28	60	30	55	50	70

SEMEN ANALYSIS

Sl. No	OP NO	Volume ml		Liquefaction Time		Fructose	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
1	I 42978	1.5	2.0	20	20	PRESENT	PRESENT
2	I 42957	1.0	2.0	30	30	PRESENT	PRESENT
3	G 95889	1.0	2.0	30	30	PRESENT	PRESENT
4	I 13253	2.0	3.0	30	30	PRESENT	PRESENT
5	H 72446	1.5	2.5	20	30	PRESENT	PRESENT
6	I 39455	1.5	1.0	30	30	PRESENT	PRESENT
7	I 41903	2.2	5.1	30	25	PRESENT	PRESENT
8	H 80572	1.5	2.0	20	30	PRESENT	PRESENT
9	H 70447	1.5	4	30	30	PRESENT	PRESENT
10	I 44256	6.5	5.9	30	30	PRESENT	PRESENT
11	I 25653	1	2.5	20	30	PRESENT	PRESENT
12	I 44516	1.5	1.5	30	30	PRESENT	PRESENT
13	I 16233	2.0	2.5	30	20	PRESENT	PRESENT
14	I 26113	2.0	3	30	35	PRESENT	PRESENT
15	I 46152	2.5	3.0	20	15	PRESENT	PRESENT
16	I 22106	3.5	3	30	30	PRESENT	PRESENT
17	F 042735	1	1	30	30	PRESENT	PRESENT
18	I 43772	1.5	2	40	40	PRESENT	PRESENT
19	I 46949	1.5	2.0	30	30	PRESENT	PRESENT
20	I 08792	2.0	2.5	25	25	PRESENT	PRESENT
21	I 17148	1.5	2.5	30	20	PRESENT	PRESENT
22	I 49209	4.0	2.5	30	30	PRESENT	PRESENT
23	I 46480	2	2.5	30	30	PRESENT	PRESENT
24	I 47208	2.5	6.5	20	8	PRESENT	PRESENT
25	I 48840	4	1.5	30	30	PRESENT	PRESENT
26	I 48490	2	2.5	30	30	PRESENT	PRESENT
27	I 29302	1.5	2.5	30	30	PRESENT	PRESENT
28	I 46426	1.5	2	30	35	PRESENT	PRESENT
29	H 86837	2	3	30	20	PRESENT	PRESENT
30	I 31859	3	2.2	30	30	PRESENT	PRESENT
31	I 51222	1.5	2.5	20	30	PRESENT	PRESENT
32	I 47764	1.5	2.5	20	30	PRESENT	PRESENT
33	I 53634	1.5	1	30	30	PRESENT	PRESENT
34	I 53597	1.5	4	30	30	PRESENT	PRESENT
35	I 52874	1.5	2.5	30	30	PRESENT	PRESENT
36	I 46955	1.5	2.5	30	30	PRESENT	PRESENT
37	H 74380	2.5	3	30	30	PRESENT	PRESENT
38	I 55296	2.5	3	30	30	PRESENT	PRESENT
39	I 22884	2	1	30	30	PRESENT	PRESENT
40	I 53967	1.5	3	20	30	PRESENT	PRESENT

URINE INVESTIGATION

SL.NO	OP NO	URINE							
		Before Treatment				After Treatment			
		Albumin	Sugar	Deposits		Albumin	Sugar	Deposits	
				Pus Cells	Epi Cells			Pus Cells	Epi Cells
1	I 42978	NIL	NIL	02-3cells	02-4 cells	NIL	NIL	02-4 cells	03-4 cells
2	I 42957	NIL	NIL	02-3cells	02-4 cells	NIL	NIL	02-4 cells	02-4 cells
3	G 95889	NIL	NIL	03-4 cells	03-3 cells	NIL	NIL	02-4 cells	02-4 cells
4	I 13253	NIL	NIL	02-4 cells	02-3 cells	NIL	NIL	03-3 cells	02-4 cells
5	H 72446	NIL	NIL	02-4 cells	02-3cells	NIL	NIL	02-4cells	03-3 cells
6	I 39455	NIL	NIL	02-4 cells	03-4 cells	NIL	NIL	02-3cells	02-4 cells
7	I 41903	NIL	NIL	03-3 cells	02-4 cells	NIL	NIL	02-3cells	02-4 cells
8	H 80572	NIL	NIL	02-3 cells	02-4 cells	NIL	NIL	03-4 cells	02-4 cells
9	H 70447	NIL	NIL	02-3cells	02-4 cells	NIL	NIL	02-4 cells	03-3 cells
10	I 44256	NIL	NIL	03-4 cells	03-3 cells	NIL	NIL	02-4 cells	02-4 cells
11	I 25653	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-4 cells	02-4 cells
12	I 44516	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	03-3 cells	02-4 cells
13	I 16233	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-3 cells	03-3 cells
14	I 26113	NIL	NIL	03-3 cells	03-3 cells	NIL	NIL	02-3cells	02-4cells
15	I 46152	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-4 cells	02-3cells
16	I 22106	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-4 cells	02-3cells
17	F 042735	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-4 cells	03-4 cells
18	I 43772	NIL	NIL	03-3 cells	03-3 cells	NIL	NIL	03-3 cells	02-4 cells
19	I 46949	NIL	NIL	02-4 cells	02-4cells	NIL	NIL	02-4cells	02-4 cells
20	I 08792	NIL	NIL	02-4 cells	03-3 cells	NIL	NIL	02-3cells	02-4 cells
21	I 17148	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-3cells	03-3 cells
22	I 49209	NIL	NIL	03-3 cells	02-4 cells	NIL	NIL	03-4 cells	02-3 cells
23	I 46480	NIL	NIL	02-4cells	02-4 cells	NIL	NIL	02-4 cells	02-3cells

URINE INVESTIGATION

SL.NO	OP NO	URINE							
		Before Treatment				After Treatment			
		Albumin	Sugar	Deposits		Albumin	Sugar	Deposits	
				Pus Cells	Epi Cells			02-3 cells	Epi Cells
24	I 47208	NIL	NIL	02-3cells	02-4 cells	NIL	NIL	02-3cells	02-4 cells
25	I 48840	NIL	NIL	02-3cells	02-4 cells	NIL	NIL	02-4 cells	03-3 cells
26	I 48490	NIL	NIL	03-4 cells	03-3 cells	NIL	NIL	02-4 cells	02-4 cells
27	I 29302	NIL	NIL	02-4 cells	02-3 cells	NIL	NIL	02-4 cells	02-4 cells
28	I 46426	NIL	NIL	02-4 cells	02-3cells	NIL	NIL	03-3 cells	02-4 cells
29	H 86837	NIL	NIL	02-4 cells	03-4 cells	NIL	NIL	02-4cells	03-3 cells
30	I 31859	NIL	NIL	03-3 cells	02-4 cells	NIL	NIL	02-3cells	02-4 cells
31	I 51222	NIL	NIL	02-3 cells	02-4 cells	NIL	NIL	02-3cells	02-4 cells
32	I 47764	NIL	NIL	02-3cells	02-4 cells	NIL	NIL	03-4 cells	02-4 cells
33	I 53634	NIL	NIL	03-4 cells	03-3 cells	NIL	NIL	02-4 cells	03-3 cells
34	I 53597	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-4 cells	02-4cells
35	I 52874	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-4 cells	02-3cells
36	I 46955	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	03-3 cells	02-3cells
37	H 74380	NIL	NIL	03-3 cells	03-3 cells	NIL	NIL	02-3 cells	02-3cells
38	I 55296	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-3cells	02-3cells
39	I 22884	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-3 cells	01-3 cells
40	I 53967	NIL	NIL	02-4 cells	02-4 cells	NIL	NIL	02-3cells	04-5 cells

DISCUSSION

There was a time when infertility was only limited to women but in present scenario male infertility is blamed in 59% of cases where couples could not conceive naturally. Most of the cases hail from IT back ground. The change in life style even among small income group has led to increase in infertility rate and lack of physical activities. . Any infections that occur at an early age in a male child and low economic standards can also lead to rise in male infertility.

The most common problems men face are low sperm count, low motility rate and morphological abnormalities. The reproductive age for men is 18 to 50

Age Distribution

Among 40 cases

45% cases are between the age group of 24-29 yrs

18% cases are between the age group of 30-34 yrs

25% cases are between the age group of 35-39 yrs

12% cases are between the age group of 40-45 yrs

Inference:

In my study the prevalence of the disease was found to be more in the age growth ranging from 24years to 29years (45%)

Occupational history

Out of 40 patients 45% patients were working in hot atmosphere.IT Profession 3Patients(7.5%),Electrician 15 Patients(37.5%) working in hot atmosphere. This plays an vital role in male infertility. This may be one of the causes for infertility.

Food habits

Out of 40 patients 36(90%) were non vegetarian and 4(10%) were vegetarian. This dietary style is more prone for developing infertility

Personal habits

Out of 40 patients 15 (37.5%) patients were smokers and Social drinkers.

10(25%) patients were only smoker.

15(37.5%) patients were with none of the above habits.

Smoking is the major cause of male infertility because it increases the concentration of free radicals in the seminal fluid.

Duration of Male Infertility

50% of patients were within 3 years duration of infertility.

25% of patients were within 4 years to 6 years of infertility.

20% of patients were within 7years to 9 years of infertility.

5% of patients were more than 10 years of infertility.

Thinai

20% of patients came from Marutham thinai.

5% of patients from Mullai thinai.

75% of patients from Neithal thinai.

Paruvakaalam

100% of the patients came in munpanikaalam(Jan-Feb). The body which is already been weak due to the effect of previous season .

Thegi

25% of patients presenting with Vatha Thegi.

50% of patients presenting with Pitha Thegi.

25% of patients presenting with Kaba Thegi.

Pitha thegi are more prone to male infertility.

Three Humors

In 50% of patients Vatham (abannan) was affected.(pre mature ejaculation, burning micturition).

In 100%of patients Pitham (Sathagam phitham) was affected. (decreased sperm count).

In 62.5% of patients Kabam (Tharpakam) was affected. (burning sensation of eyes).

KOSAM (Five sheaths)

In 100%of the patients Annamayakosam was affected. (Two of the physical constituents saaram and senner affected).

80% of the patients ManomayaKosam was affected.(depression).

100%of the patients AnandhamayaKosam was affected.(decreased sperm count and motility).

Udal Thathukkal

Saram was affected in 100% patients.

Senneer was affected in 100% patients.

Sukkilam was affected in 100% patients

Derangement of Saaram, Senneer,sukkilam or any one of this lead to development of infertility.

Envagai theryu

Naa -7.5% of patients presenting with Dryness of tongue.

Sparisam – Sparisam was Veppam in 32.5%patients due to working in hot atmosphere.

Sparism was Methavepam in 67.5%patients.

Moothiram was affected in 42.5% patients (burning micturition).

Naadi -37.5% of the patients were presenting with Vatha Pitham Naadi.

62.5% of the patients were presenting with Pitha Vatham Naadi.

Sukkilam:

Buoyancy on water : The important Siddha parameter to evaluate the Sperm.In 5% of the patients sperm were floating on water indicating abnormal condition. 95% of the patients presented sperms not were floating on water indicating normal condition.

Neerkuri

The important Siddha diagnostic parameter.

30% of patients the colour of the urine was pale yellow colour.

10% of the patients the colour of the urine was colour.

10% of the patients the colour of the urine was dark yellow in colour.

50% of the patients the colour of the urine was straw coloured urine.

Neirkuri

An important Siddha parameter reflecting the signs of Prognosis is spreading pattern of the in the urine .

10% of patients the Nei kuri showed slowly spread pattern.

75% of patients the Nei kuri showed fastly spread pattern.

15%% of patients the Nei kuri showed Stand still(No spread)

History of Masturbation

Masturbation habit was present in 40 patients Out of these 75% were within 5 years duration. 25% were above 5 years to 10 years duration.

In all the 40 patients the frequency of masturbation was once in 2 days or weekly twice.

Clinical Features

Premature ejaculation is the commonest symptom in infertility patients. 75% of patients suffered with this complaint. These patients were not fully satisfied during intercourse. 70% the patients were improved after the treatment.

87.5% Patients came with erectile dysfunction , but not persistent. All the 80% patients improved after the treatment . sometimes premature ejaculation and erectile dysfunction may be associated with painful coitus.

12.5%Patients came with painful micturition.7.5% the patients were improvement after treatment.

Nocturnal emission is another important feature in infertility. Recurrent emission leads to decreased sperm count and motility. 25% patients came with this complaint, among them 20% were improved after the treatment.

Semen analysis- Semen Count After treatment improvement profile

5% of patients improved after treatment within 5 Million / ml

5% of patients improved after treatment more than 5Million to 10Million.

10% of patients improved after treatment more than 11Million to 20Million.

20% of patients improved after treatment more than 21Million to 30Million

60% of patients improved after treatment more than 30 Million

Semen analysis - Active Motility After treatment improvement profile

15% of patients improved after treatment with Active Motility less than 5%

25% of patients improved after treatment with Active Motility more than 5% to 10%.

20%of patients improved after treatment with Active Motility more than 11% to 20%.

2.5% of patients improved after treatment with Active Motility more than 21% to30%.

37.5%of patients improved after treatment with Active Motility more than 30%.

PRIMARY OUTCOME OF THE TREATMENT WITH THE TRAIL DRUG POONAKALI VITHAI CHOORNAM

Primary out come regarding sperm count

50.5% of the patients falling into the category **GOOD**- increase of sperm count with range of 40-60Million/ml.

12.5% of the patients falling into the category **MODERATE**- increase of sperm count with range of 40 to more than 50Million/ml.

12.5% of the patients falling into the category **MILD**- increase of sperm count with range of 40-upto 50Million/ml.

24.5% of the patients falling into the category **POOR**- with the range of sperm count below 40Million/ml.

Primary out come regarding Active Motility

24% of the patients falling into the category **GOOD**- increase of Active Motility with range of 50%-70%.

41% of the patients falling into the category **MODERATE**- increase of Active Motility with range of 50 %to 60%.

10% of the patients falling into the category **MILD**- increase of Active Motility with range of with 50%.

25% of the patients falling into the category **POOR**- with range of Active Motility within 50%.

In clinical study , out of 40 patients 37 patients were showed improvement in clinical lab investigation(semen analysis). The sperm count and sperm motility were improved in those patients. All the 37 patients were relived from clinical symptoms.

The sperm count and sperm motility differences before and after treatment showed statistically significant in Male infertility patients.

STATISTICAL ANALYSIS:

BIO STATISTICAL ANALYSIS

The effectiveness of the clinical trialdrug Poonaikali vithai choornam was assessed by using paired comparison test (paired t test). The responses regarding sperm count and motility of the patients to the drug are analyzed

Assessment of the effectiveness of drug:

The effectiveness of the drug was assessed by the improvement of the patients from low sperm count, low motility which is measured using assessment score.

Inference: The test drug is statistically significant ($p>0.0001$) and hence it is effective in the treatment of Aanmaladu.

BIOCHEMICAL ANALYSIS:

- Preliminary Biochemical analysis of poonaikali vithai choornam was done in NIS biochemical analysis showed the presence of minerals like,chloride, carbonate, iron, calcium, ammonium, potassium.

TOXICITY STUDY:

ACUTE TOXICITY:

Acute toxicity studies done in C.L.Baid Meyha college as per OECD guide lines revealed the safety of the drug in oral single doses(2000mg) it did not produce any adverse effects in the animals. There were no abnormalities detected in the internal organs on necropsy.

(28 days)REPEATED ORAL TOXICITY:

28 days Repeated oral toxicity studies done in National Institute of Siddha, as per OECD guide lines did not reveal any adverse effects in the animal. Animal behavior, metabolic functions (food and water intake, defecation, urination etc) did not reveal any abnormality. Blood investigation parameters and histopathological examination did not show any abnormal variations.

Hence it can be concluded from the study that up to maximum dose (2000 mg/animal) the drug was proved to be safe.

There were no side effects were observed during the course of treatment and after treatment also.

SUMMARY

In developing country like India ,one in every four couples found to be affected by infertility. In 2010 almost 50 million couples world wide unable to have a child after five years of marriage. Infertility rate has hardly changed over the past 20 years.The global health community has made great success in improving the infertility care in the past decade. Infertility can lead to distress and depression as well as discrimination and ostracism. infertility can be caused by poor sexual life style habits that are easily remedied. Heavy usage of alcohol, tobacco drugs, tight underwares or pants which raise the scrotal temperature and reduce the sperm count. Infections play an vital role in male infertility that block the ducts through which the sperm travels. Exposure to metals such as lead, chemical and pesticide plays a major role in male infertility.Auto immunity in which antibodies or cells of the human immune system attack sperm cells mistaking them as toxic invaders. Now a days male infertility treatmeant is a challenging task. In recent years siddha system of medicine have bloomed up in treating male infertility with high success rate.

The main aim of this study is to document the effectiveness of siddha medicine poonaikali vithai choornam (Internal medicine) in the management of AANMALADU (Male infertility).

The objective of this study is the Preclinical and Clinical Studies .Preclinical studies consist standardisation and safety of the study of drug.Clinical studies conducted in 40 cases.

The raw drug were purchased from reputed country medical shop in Chennai and drug authentication by Botanical of NIS.

The drug was prepared as per standard operating procedure mentioned in the siddha literature in Gunapadam laboratory of National Institute of Siddha.

The standardization of study drug was carried out in the Biochemistry lab of NIS.It revealed the presence of **chloride, fluoride, carbonate** with the study drug.

The preclinical toxicity studies (Acute and repeated oral 28 days toxicity) for the above said study drug was conducted at Pharmacology laboratory, C.L.Baid Metha college (**IAEC NO:** IAEC/XLIX/13/CLBMCP/2016**).**

The study drug was found to the usage as per the data generated from the studies.

The histopathological studies did not reveal any abnormalities in the animals in both control and test group revealed that the drug was non-toxic.

The clinical study was conducted with a well defined protocol and a proper proforma after getting the approval of the Institutional Ethical Committee. **(IEC NO:NIS/IEC/9/2014-15/7-26.08.2015.**

The study data were registered in CTRI (Clinical Triall Registry of India) with **ID NO: CTRI/2016/07/011882.**

After screening 60 cases study based on the inclusion criteria and exclusion criteria reporting at the OPD of Maruthuvam , 40 cases were selected for induction to the study. Before enrolment into the trial the informed consent was obtained from the patients.

The aim of the study is to increase the sperm count and sperm motility in male infertility patients. The duration of administration of study drug 48 days. The study drug dose was 6grams twice a daily with cow ghee.

Before Starting the treatment semen analysis, routine blood and urine examination were taken in all 40 patients. Siddha methods like three Humor, Thegi, Kosangal, udal thathukkal, Envagai thervu,neeikuri, nerkuri and buoyancy of Semen on water were analysed in all 40 Cases.Out of 40 Patients 30 Patients Presence with following Symptoms Premature ejaculation, Erectile dysfunction, Painful micturition, Nocturnal emission.The remaining 10 Patients were symptoms free but their clinical lab semen analysis report showed low sperm count and motility problem with The entire details were noted in the selection proforma.

Patients were instructed to come for clinical once in 12 days. They were also instructed to bring back the unconsumed drug during the next visit and return the same.In every visit the clinical assessment was made.

At the end of the treatment reduction of clinical symptoms and improvement in clinical lab para meters (Sperm count and motility)in all the 40 patients.

Improvement in the Sperm count with in 5 million and more than 5 to 10 million were report in cases each 5%. More than 11 to 20 million was found in cases 10%. More than 21 to 30 million was found in 20% of cases. More than 30 million was reported in 60% of cases.

Improvement in the active motility with the range of 50%-70% in 24% of cases. 50%-60% in 41% of cases. 50% in 10% of cases. Lessthan 50% in 25% of cases were observed.

30patients complaining regarding secondary sexual characters showed improvement. 18 patients attained the stage of fertilization. After the treatment no side effects were noted.

The cost of medicine is comparatively low. The ingredients were easily available and the rural people will be benefited more.

I have concluded the siddha medicine Poonaikali vithai choornam was effective in treatment of "Aan maladu" (Male infertility especially oligospermia and asthenozoospermia).

CONCLUSION

The trail drug POONAIKALI VITHAI CHOORNAM on administrating to 40 patients for 48days have improved the quality of semen in count and motility.

The safety studies (Acute toxicity and repeated oral toxicity) studies conducted revealed that the study drug was safe even at higher dosage of 2000 mg/kg body weight in Wistaralbino rats as per OECD guideline-423

Expenditure of the study drug is cost effective, easily preparable and highly effective in Aan maladu.

Sperm Count: (Ref: As per 1999 WHO criteria**)**

Sperm count have improved to Good result by 50.5%

Sperm count have improved to Moderate by 12.5%

Sperm count have improved to Mild by 12.5%

Sperm count falling with the Poor criteria by 24.5%

Sperm Motolity: (Ref: As per 1999 WHO criteria**)**

Sperm motility have improved to Good result by 24%

Sperm motility have improved to Moderate by 41%

Sperm motility have improved to Mild by 10%

Sperm motility falling with the Poor criteria by 25%

- Initially 50% of patients were affected from secondary sexual characters like premature ejaculation,erectile dysfunction,nocturnal emission,Painful micturition.Among them 44.4% were improved after the treatment.
- No adverse drug reactions were noticed during the course of treatment
- Because of the encouraging clinical and laboratory results, the study may be undertaken with the same medicines for a prolonged period in a large number of cases for the treatment of Aan maladu.

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NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 47

AYOTHIDOSS PANDITHAR HOSPITAL
DEPARTMENT OF MARUTHUVAM
PRE CLINICAL AND CLINICAL STUDY ON "AAN MALADU " (MALE INFERTILITY)

AND THE DRUG OF CHOICE IS "POONAIKALI VITHAI CHOORANAM"

FORM I SCREENING & SELECTION PROFORMA

REG NO:
1. STUDY NO_____ 2 OP NO:_____

3.NAME :_____ 4. AGE/SEX_____5.RELIGION : H / C / M / O

6.OCCUPATION / INCOME : _____

INCLUSION CRITERIA

1. Male infertility
2. Age 21- 45 year
3. Maritial status - more than 1 year
4. Sperm count <40 Millions/Ejaculation
5. Motility less than < 50 %
6. Patient willing to sign the informed consent stating that he will conscientiously stick to the treatment during 48days but can opt out of the trial of his own conscious discretion.
7. Patients who are willing to give specimen of blood , urine and semen before and after the treatment

EXCLUSION CRITERIA

1. Azoospermia
2. Hydrocele
3. Diabetes mellitus
4. Endocrine disorders
5. Hypertension
6. Caridiac diseases
7. VDRL & STD
8. Inguinal Hernia
9. Renal diseases
10. Varicose veins
11. Systemic illness

ADMITTED TO TRAIL : YES ☐ NO ☐ If Yes Serial NO:
Date:

Station:

Signature of the Investigator:

Signature of the Lecturer:

Signature of the HOD

NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 47
AYOTHIDOSS PANDITHAR HOSPITAL
DEPARTMENT OF MARUTHUVAM

PRE CLINICAL AND CLINICAL STUDY ON "AAN MALADU " (MALE INFERTILITY) AND THE DRUG OF CHOICE IS "POONAIKALI VITHAI CHOORANAM"

FORM lI CLINICAL RESEARCH FORM

REG NO:

1. Study No :_____ 2. OP No:_____

3. Name: _____ 4. Gender: Male

5. Age (years): _____DOB ☐☐ ☐☐ ☐☐☐☐
Date Month Year

6.Address:_____ _____
_____ _____

7.A.Occupation:---------- B. Nature of work----------

8. Educational Status: A) Illiterate ☐ B)Literate ☐ 9.Marital status-

10. Complaints and Duration:

_____

_____

11. Habits of

A) Smoking	1. Yes; duration _____ years;	Number - 2.No
B) Alcoholism	1. Yes; duration _____ years;	Quantity- ml 2.No
C) Tobacco chewing	1. Yes; duration _____ years;	2.No
D) Betel chewing	1. Yes; duration _____ years;	2.No
E)Drugs addiction	1. Yes; duration _____ years;	2.No

12.Dietary style A.Pure vegetarian ☐ B.Non-vegetarian ☐ C. Mixed diet ☐

13.Treatment History:

Had the patient been treated before with fertility drugs? A)Yes ☐ B)No ☐

14.Previous history:

Past Infertility history (Yes/No)

Past Medical history (Yes/No)

Past Surgical history (Yes/No)

SIDDHA SYSTEM OF EXAMINATION

1. ENNVAGAI THERVU: [EIGHT-FOLD EXAMINATION]

I. NAADI: [PULSE PERCEPTION]

Naadi	0^{th} day	12^{th} Day	24^{th} Day	36^{th} Day	48^{th} Day
Vali					
Azhal					
Iyyam					
Vali azhal					
Azhal vali					
Iyya vali					
Vali Iyyam					
Azhal Iyyam					
Iyya Azhal					

II. NAA:[TONGUE]

	0th Day	12th Day	24th Day	36th Day	48th Day
Colour	Dark / Yellow/ Red / Pale/ Normal	Dark / Yellow/ Red / Pale/ Normal	Dark / Yellow/ Red / Pale/ Normal	Dark / Yellow/ Red / Pale/ Normal	Dark / Yellow/ Red / Pale/ Normal
Taste	Sweet/ Bitter / Sour Pungent/ None	Sweet/ Bitter / Sour Pungent/ None	Sweet/ Bitter / Sour Pungent/ None	Sweet/ Bitter / Sour Pungent/ None	Sweet/ Bitter / Sour Pungent/ None
Coating	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent
Fissure	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent
Saliva	Normal/ Increased/ Decreased	Normal/ Increased Decreased	Normal/ Increased/ Decreased	Normal/ Increased/ Decreased	Normal/ Increased/ Decreased
Dryness	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent
Glossitis	Present/ Absent	Present /Absent	Present/ Absent	Present/ Absent	Present/ Absent
Baldness	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent

III.NIRAM: [COMPLEXION]

0^{th} Day	12th day	24^{th} Day	36^{th} Day	48^{th} Day
Dark/ Yellowtinted/ Wheatish brown/ Pale	Dark/ Yellowtinted/ Wheatish brown/ Pale	Dark/ Yellowtinted/ Wheatish brown/ Pale	Dark/ Yellowtinted/ Wheatish brown/ Pale	Dark/ Yellowtinted/ Wheatish brown/ Pale

IV.MOZHI: [VOICE]

0^{th} Day	12th day	24^{th} Day	36^{th} Day	48^{th} Day
Medium/ High/ Low pitched	Medium/ High/ Low pitched	Medium/ High/ Low pitched	Medium/ High/ Low pitched	Medium/ High/ Lowpitched

V.VIZHI: [EYES] (Lower palpabrel conjunctiva)

0th Day	12th day	24th Day	36th Day	48th Day
Yellow Red / Pale/Normal	Yellow Red/ Pale/Normal	Yellow Red/ Pale/Normal	Yellow Red/ Pale/Normal	Yellow Red/ Pale/Normal

VI. MALAM; [BOWEL HABITS / STOOLS]

	0th Day	12th Day	24th Day	36th Day	48th day
Colour	Dark/ Yellow/ Pale/Others	Dark/ Yellow/ Pale/Others	Dark/ Yellow Pale/Others	Dark/ Yellow/ Pale/Others	Dark/ Yellow/ Pale/Others
Consistency	Solid/ Semisolid Watery	Solid/ Semisolid Watery	Solid/ Semisolid Watery	Solid/ Semisolid Watery	Solid/ Semisolid Watery
Stool bulk	Normal/ Reduced	Normal /Reduced	Normal/ Reduced	Normal/ Reduced	Normal/ Reduced
Constipation	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent
Diarrhoea	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent

NEER KURI	**0th Day**	**12th Day**	**24 th Day**	**36th Day**	**48th day**
Niram [Colour]	White/ Yellowish/ Straw coloured/ Crystal clear	White/ Yellowish/ Straw coloured/ Crystal clear	White/ Yellowish/ Straw coloured/ Crystal clear	White/ Yellowish/ Straw coloured/ Crystal clear	White/ Yellowish/ Straw coloured/ Crystal clear
Manam [Odour]	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent
Nurai [Froth]	Nil/ Reduced/ Increased	Nil/ Reduced/ Increased	Nil/ Reduced/ Increased	Nil/ Reduced/ Increased	Nil/ Reduced/ Increased
Edai [Sp.gra]	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced
Enjal [Deposits]	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent	Present/ Absent
Volume	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced	Normal/ Increased/ Reduced

VII. URINE EXAMINATION:

NEIKURI	**0th day**	**12th day**	**24th day**	**36th day**	**48th day**
Serpentine fashion					
Annular/Ringed fashion					
Pearl beaded fashion					
Mixed fashion					
Other fashion					

VIII. SPARISAM: [PALPATORY PERCEPTION]

0th Day	12th Day	24th Day	36th Day	48th day
Warmth/ Cold/ Normal/ Sweat	Warmth/ Cold/ Normal/ Sweat	Warmth/ Cold/ Normal/ Sweat	Warmth/ Cold/ Normal/ Sweat	Warmth/ Cold/ Normal/ Sweat

THEGI: [TYPE OF BODY CONSTITUTION]

Vatham predominant		Kabam predominant
Pitham predominant		Thondha udal

6.NILAM: [LAND WHERE PATIENT LIVED MOST]

1.Kurinji (Hilly terrain) ☐

2.Mullai (Plains) ☐

3.Marutham (Forestrange) ☐

4.Neithal (Coastal belt) ☐

5.Palai (Aridregions) ☐

7.KAALAM

Kaarkalam ☐ Pinpanikalam ☐

Koothirkalam ☐ Ilavenil ☐

Munpanikalam ☐ Muthuvenil ☐

8. GUNAM

Sathuvam ☐ Rasatham ☐ Thamasam ☐

IMPORIGAL (SENSORY ORGANS)

	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Mei (Skin)					
Vaai (Buccal Cavity)					
Kann (Eye)					
Mooku (Nose)					
Sevi(Ear)					

KANMENTHIRIYAM (MOTOR ORGANS)

Kanmenthiriyam	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Kai (upper limb)					
Kaal (lower limbs)					
Vaai (buccal cavity)					
Eruvai (excretory organs)					
Karuvai (reproductive organs)					

KOSANGAL(Sheath)

Kosangal	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Annamaya Kosam					
Pranamaya kosam					
Manomaya kosam					
Vignanamaya kosam					
Ananthamaya kosam					

MUKKUTRAM:[AFFECTION OF THREE HUMORS]
A)VATHAM:

Vatham	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Praanan					
Abaanan					
Samaanan					
Udhaanan					
Viyaanan					
Naagan					
Koorman					
Kirukaran					
Devathathan					
Dhananjeyan					

B) PITHAM:

Pitham	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Analapitham					
Prasakam					
Ranjakam					
Aalosakam					
Saathakam					

C) KABAM:

Kabam	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Avalambagam					
Kilethagam					
Pothagam					
Tharpagam					
Santhigam					

13. SEVEN DHATHUS: (7 SOMATIC COMPONENTS)

Udal thathukkal	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Saaram[Chyme]					
Senneer[Blood]					
Oon[Muscle]					
Kozhuppu[Fat]					
Enbu[Bones]					
Moolai [Bonemarrow]					
Sukkilam/Suronitham[Genital discharges]					

14. GENERAL EXAMINATION:

General Examination:	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Height (cms)					
Weight (kg)					
Temperature(°F)					
Pulse rate (pe rmin)					
Heart rate (per min)					
Respiratoryrate(permin)					
Blood pressure(mm/Hg)					
Pallor					
Jaundice					
Cyanosis					
Lymphadenopathy					
Pedal edema					
Clubbing					
Jugular venous pulsation					

15. SYSTEMIC EXAMINATION:

Systemic examination	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
Locomotor system					
Cardio Vascular System					
Respiratory system					
Gastro Intestinal system					
Central Nervous System					
Urogenital system					
Endocrine System					

16.Examinatiin Of Male Genitalia

	Testis	Epididymis	Vas deferens	Varicocele	Hydrocele	Hernia
Right						
Left						

Examination of penis

Prepuce	External urethral meatus	Glans penis	Body of penis

17. CLINICAL SYMPTOMS

S.no	CLINICAL SYMPTOMS	0^{th} day	12^{th} day	24^{th} day	36^{th} day	48^{th} day
1	Premature ejaculation					
2	Nocturnal emission					
3	Erectile dysfunction					
4	Painful coitus					
5	Painful micuturition					

Date :

Station:

Signature of the Investigator:

Signature of the Lecturer:

Signature of the HOD

NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 47

AYOTHIDOSS PANDITHAR HOSPITAL

DEPARTMENT OF POTHUMARUTHUVAM

PRE CLINICAL AND CLINICAL STUDY ON "AAN MALADU " (MALE INFERTILITY) AND THE DRUG OF CHOICE IS "POONAIKALI VITHAI CHOORANAM "

FORM III
LABORATORY INVESTIGATION ON ENROLLMENT

1. STUDY NO_____ 2 OP NO_____: REG NO:

3. NAME_____ 4.DATE OF ASSESSMENT :----------

BLOOD INVESTIGATION		NORMAL VALUES	BEFORE TMT	AFTER TMT
HB(gms%)		M:13-18 W:11-16		
T.RBC(million cells /cu.mm)		M:4.5-6.5 W:3.5-5.5		
ESR (mm)	½ hr.	M:0-10 W:0-20		
	1 hr.			
T.WBC (cells /cu.mm)		4000-11000		
DIFFERENTIAL COUNT (%)	Polymorphs	40-75		
	Lymphocytes	20-35		
	Monocytes	2-10		
	Esonophils	1-6		
	Basophils	0-1		

Blood Investigation		Normal Values	Before TMT Date:	After TMT Date
Blood glucose (mg/dl)	Fasting	70-100		
	PP	80-140		
	Random	100-140		
Lipid profile (mg/dl)	Serum cholesterol	150-250		
	HDL	30-60		
	LDL	Upto 130		
	VLDL	40		
	TGL	Upto 160		
RFT (mg/dl)	Blood urea	16-50		
	Serum creatinine	0.6-1.2		
	Serum Uric acid	M:3-9 W: 2.5-7.5		
LFT (mg/dl)	Total bilirubin	0.3-1		
	Direct bilirubin	0.1-0.3		
	Indirect bilirubin	0.2-0.8		
	Serum total protein	6-8		
	Serum Albumin	3.5-5.5		
	Serum globulin	2-3.5		
	Serum calcium	9-11		
	Serum phosphorous	2-5		
	SGOT (IU/L)	6-18		
	SGPT (IU/l)	3-26		
	Alkaline phosphatase mg/dl	3-12		

Special investigation:

Semen analysis:

	Before TMT(with Date)	After TMT (With Date)
Volume		
Colour		
Apperance		
Viscosity		
Liquefaction time		
Fructose		
Sperm count		
Motility		
Morphology		

URINE INVESTIGATION	Before TMT(with Date)	After TMT (With Date)
Albumin		
Fasting sugar		
PP sugar		
Random Sugar		
Deposits		
Bile salts		
Bile pigments		
NEIKURI		
MOTION TEST		
Ova		
Cyst		
Occult blood		

Date :
Station:
Signature of the Investigator: Signature of the HOD

Signature of the Lecturer:

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

PRE CLINICAL AND CLINICAL STUDY ON "AAN MALADU " (MALE INFERTILITY) AND

THE DRUG OF CHOICE IS "POONAIKALI VITHAI CHOORANAM"

FORM - IV (DRUG COMPLIANCE FORM)

NAME:

DRUG NAME:

On 1st day-Date: Drugs issued: Drugs returned:

On 12th day-Date: Drugs issued: Drugs returned:

On 36th day-Date: Drugs issued: Drugs returned:

On 48th day-Date: Drugs issued: Drugs returned

Day	Date	Morning	Evening	Day	Date	Morning	Evening
Day 1				Day25			
Day2				Day26			
Day3				Day27			
Day4				Day28			
Day5				Day29			
Day6				Day30			
Day7				Day31			
Day8				Day32			
Day9				Day33			
Day10				Day34			
Day11				Day35			
Day12				Day36			
Day13				Day37			
Day14				Day38			

Day15				Day39			
Day16				Day40			
Day17				Day41			
Day18				Day42			
Day19				Day43			
Day20				Day44			
Day21				Day45			
Day22				Day46			
Day23				Day47			
Day24				Day48			

Date:

Station:

Signature of the Investigator:

Signature of the Lecturer:

Signature of the HOD

தேசிய சித்த மருத்துவ நிறுவனம், சென்னை 47
அயோத்திதாசர் பண்டிதர் மருத்துவமனை
ஆண் மலடு நோய்க்கான சித்த மருந்தின் (**"பூனைகாலி விதை சூரணம்"**) பரிகரிப்புத்

திறனைக் கண்டறியும் மருத்துவ ஆய்விற்கான தகவல் படிவம்.

FORM - V தகவல் படிவம்

முதன்மை ஆராய்ச்சியாளர் பெயர் **மரு.கி.இராஜேந்திரன்**
நிறுவனத்தின் பெயர் : தேசிய சித்த மருத்துவ நிறுவனம்
தாம்பரம் சானடோரியம்
சென்னை- 47

மரு.கி.இராஜேந்திரன் ஆகிய நான் தேசிய சித்த மருத்துவமனையில் பட்ட மேற்படிப்பு பயின்று வருகிறேன். ஆண் மலடு என்பது குழந்தைபேறு உருவாக்க முடியாத நிலையாகும், விறைப்புத் தன்மை குறைவு, கனவிற் விந்து கழிதல், வலியுடன் கூடிய உறவு, விந்து முந்துதல், ஆகிய குறிகுணங்கள் காணும். இந்நோய்க்கு தேசிய சித்த மருத்துவமனையில் பல சித்த மருந்துகள் பயன்படுத்தப்பட்டு வருகின்றது. சித்த மருத்துவ பட்ட மேற்படிப்பில், ஆய்வின் ஒரு பகுதியாக புதிய மருந்துகளை பயன்படுத்தும் நோக்கில் **பூனைகாலி விதை சூரணம்** இந்நோய்க்கு வழங்க பரிந்துரை செய்கிறேன். இந்த மருந்தின் செய்முறை, அளவு, அனுபானம் மற்றும் மருத்துவ பயன்கள் அனைத்தும் அங்கீகரிக்கப்பட்ட சித்த மருத்துவ நூலில் கூறப்பட்டுள்ளது. எந்தவித கட்டணமுமின்றி தாங்கள் இந்த மருந்தினை பெற்றுக்கொள்ளலாம். இந்த ஆய்வில் மருந்து உட்கொள்ளும் காலம் 48நாட்கள் ஆகும். 48 நாட்களுக்கு தொடர்ந்து பத்தியம் காக்க வேண்டும், இம்முறைப்படி வெளி நோயாளர்கள் 12 நாட்களுக்கு ஒரு முறை மருத்துவமனைக்கு வரவேண்டும். 48நாட்கள் மருந்து உட்கொள்ளும் காலம் முடிந்த பிறகு நோய்க்கான குறிகுணங்கள் மற்றும் ஆய்வக பரிசோதனைகள் இவற்றின் முடிவுகளின் அடிப்படையில் மருந்தின் பரிகரிப்புத்திறன் கண்டறியப்படும்.

இந்த ஆய்வு சம்பந்தமாக சில கேள்விகளை தங்களிடம் கேட்க இருக்கிறேன். தங்களிடமிருந்து பெறப்படும் கருத்துக்கள் மற்றும் குறிப்புகள் அனைத்தும் நம்பிக்கையாக பதிவு செய்யப்படும். இந்த ஆய்வில் தங்களை உட்படுத்திக்கொள்வதின் மூலம் எந்த வகையிலும் பாதிப்புக்குள்ளாக மாட்டீர்கள் என உறுதி அளிக்கிறேன்.எந்தவித வற்புறுத்தலுமின்றி, இந்த ஆய்வில் பங்கேற்கவும், இந்த ஆய்வு சம்பந்தமாக கேட்கப்படும் கேள்விகளுக்கு பதில் கூறவும் தங்களுக்கு முழு சுதந்திரம் அளிக்கப்படுகிறது. இந்த ஆய்வில் பங்கேற்பதற்கு எந்த சன்மானமும் வழங்கப்படமாட்டாது. ஆனால், ஆய்வு முழுவதும் எனது மேற்பார்வையிலும், தங்கள் உடல்நலன் குறித்த தனி கவனத்திலும் ஆய்வு மேற்கொள்ளப்படும். ஆண் மலடு நோய்க்கான புதிய மருந்தின் பரிகரிப்புத்திறனை சமூகத்திற்கு உணர்த்தும் வகையில் இந்த ஆய்வு மேற்கொள்ளப்படுகிறது, இந்த ஆய்வில், மருந்து உட்கொள்ளும் காலத்தில் மாறுபட்ட குறிகுணங்கள் தொடர்ந்து இருக்கும் பட்சத்தில், முதன்மை ஆராய்ச்சியாளரான என்னிடம் தெரிவிக்கப்பட்டு, தேசிய சித்த மருத்துவமனையில் அதற்க்கான தீர்வு வழங்கப்படும். இந்த ஆய்வினைத் தொடர தங்களுக்கு விருப்பம் இல்லையெனில், எப்பொழுது வேண்டுமானலும் ஆய்வின் இடையில் விலகிக்கொள்ள முழு சுதந்த்திரம் தங்களுக்கு உண்டு. மேலும் மருத்துவமனையில் வழங்கப்படும் இந்நோய்க்கான வழக்கமான மருந்துகளை பெற்றுக்கொள்ளவும் அறிவுறுத்தப்படுகிறீர்கள்.

இந்த ஆய்வில் சேகரிக்கப்படும் விபரங்கள் அனைத்தும் தங்களுக்கும் முதன்மை ஆராய்ச்சியாளரான எனக்கும் இடையில் இரகசியமாக வைக்கப்படும். கேள்வி பதில் வடிவத்தில் தங்களிடம் கேள்விகள் கேட்கப்படும். பிற சோதனை படிவங்களிலும்

தங்களின் பெயர் தவிர்க்கப்பட்டு ஆய்வாளரால் தங்களுக்கென தனிக் குறியீடு வழங்கப்படும். அந்தக் குறியீடு ஆய்வாளருக்கு மட்டுமே தெரிந்ததாக இருக்கும். நீங்கள் இந்த ஆய்வில் பங்கேற்க விருப்பப்பட்டால், திட்ட வரைவு தகவல் படி தேர்வு செய்யப்படுவீர்கள்.

நீங்கள் இந்த ஆய்வில் பங்கேற்கும் முன், இந்த ஆய்வினைப் பற்றிய மேலும் விபரங்கள் பெற வேண்டுமென விருப்பப்பட்டால், இந்த ஆய்வின் முதன்மை ஆராய்ச்சியாளர் மற்றும் தேசிய சித்த மருத்துவமனை, பட்ட மேற்படிப்புத்துறை மாணவர் **மரு.கி.இராஜேந்திரன்** ஆகிய என்னை 8807565295 என்ற எண்ணில் தொடர்பு கொள்ளலாம். மேலும், நீங்கள் இந்த ஆய்வில், உங்களது பங்கேற்பு மற்றும் உரிமை பற்றி தெரிந்து கொள்ள தேசிய சித்த மருத்துவமனை, தலைவர்/செயற்க்குழு உறுப்பினர் அவர்களையும் 91-44-22411611 என்ற எண்ணில் தொடர்பு கொள்ளலாம்.

NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 47

AYOTHIDASAR PANDITHAR HOSPITAL
DEPARTMENT OF MARUTHUVAM
Preclinical and Clinical Study on AAN MALDU (MALE INFERTILITY)and the drug of choice is "Poonaikali vithai chooranam"

FORM V – INFORMATION SHEET

Name of the Principal Investigator : Dr.K.Rajendran
Name of the Institution : National Institute of Siddha, Tambaram Sanatorium, Chennai-47.

Dr.K.Rajendran Studying M.D(S) in National Institute of Siddha, Chennai. The disease called AAN MALDU(male infertile) symptoms like premature ejaculation, erectile dysfunction, nocturnal emission, painful coitus, painful micturition This condition is being treated in NIS with many siddha formulations. As a part of M.D(S) research programme and developing new efficacious medicines, I propose to study the **Poonaikali vithai chooranam** formulation for treating the condition. This formulation has been mentioned in siddha literature and empirical evidence with contemporary tools are required for documentation. You can receive medicines at free of cost.**"Poonaikali vithai chooranam"**can be taken twice daily with milk 48 days. The diagnosis tests will be carried out at free of cost. I will assess the effect of treatment after completion of 48 days of treatment using clinical and lab parameters.

- In this regard, Ineed to ask you few questions. I will maintain confidentiality of your comments and data obtained from you. There will be no risk of disclosing your identity and no physical, psychological or professional risk is involved by taking part in this study.

- Taking part in this study is voluntary. No compensation will be paid to you for taking part in this study. You can choose not to answer any specific question. There is no specific benefit for you if you take part in the study, but you will be under our clinical monitoring and specific attention will be given for your health. Taking part in the study may be of benefit to the community, as it may help us to develop medicine for aan maldu. In case of any adverse symptoms which is expected for few .patients during the treatment, shall be reported to Principle investigator and care will be taken in NIS for relief. You can withdraw from the study at the midst of treatment period, if you are not interested to continue and you will receive our regular out patient treatment without any condition.

- The information we will collect in this study, will be kept confidential remain between you and the principal investigator. We will ask you a few questions through questionnaire. I will not write your name on other investigation forms which we will sent for different investigating/analysis sections and we will use a code instead given by the principal investigator. Only the principal investigator

will know the key to this code which will be kept in safe custody. If you agree to be a participant in this study, you will be screened as per the study protocol.

- If you wish to find out more about this study before taking part, you can ask me all the questions you want or contact Dr.K.Rajendran PG scholar (Mobile phone no:8807565295 cum principal investigator of this study, attached to the National Institute of Siddha, Chennai. You can also contact the Chairman/Member-secretary of Ethics committee, National Institute of Siddha, Chennai – 600047, Tel no: 91-44-22411611, for rights and participation in the study.

NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 47
AYOTHIDASAR PANDITHAR HOSPITAL

DEPARTMENT OF POTHUMARUTHUVAM

PRE CLINICAL AND CLINICAL STUDY ON "AAN MALADU " (MALE INFERTILITY) AND THE DRUG OF CHOICE IS "POONAIKALI VITHAI CHOORANAM

FORM VII ADVERSE DRUG REACTION FORM / PHARMACOVIGILENCE FORM

1. STUDY NO_____ 2 OP NO_____: **REG** NO: 321411207/2014-17

3. NAME_____ 4.DATE OF ASSESSMENT :----------

NATIONAL PHARMACOVIGILANCE PROGRAMME FOR SIDDHA DRUGS

Reporting Form for Suspected Adverse Reactions to Siddha Drugs

Please note: i. All consumers / patients and reporters information will remain confidential.

ii. It is requested to report all suspected reactions to the concerned, even if it does not have complete data, as soon as possible.

Peripheral Center code: State:

1. Patient / consumer identification (please complete or tick boxes below as appropriate)

Name	Father name	Patient / Record No.
Ethnicity	Occupation	
Address Village / Town Post / Via District / State		Date of Birth / Age:
		Sex: Male / Female Weight : Degam:

2. Description of the suspected Adverse Reactions (please complete boxes below)

Date and time of initial observation		Season:
Description of reaction		Geographical area:

3. List of all medicines / Formulations including drugs of other systems used by the patient during the reporting period:

Medicine	Daily dose	Route of administration & Vehicle - Adjuvant	Date		Diagnosis for which medicine taken
			Starting	Stopped	
Siddha					
Any other system of medicines					

4. Brief details of the Siddha Medicine which seems to be toxic :

Details	Drug – 1	Drug – 2	Drug – 3
a) Name of the medicine			
b) Manufacturing unit and batch No. and date			
c) Expiry date			
d) Purchased and obtained from			
e) Composition of the formulation / Part of the drug used			

b) Dietary Restrictions if any
c) Whether the drug is consumed under Institutionally qualified medical supervision or used as self medication.
d) Any other relevant information.

5. Treatment provided for adverse reaction:

6. The result of the adverse reaction / side effect / untoward effects (please complete the boxes below)

Recovered:	Not recovered:	Unknown:	Fatal:	If Fatal Date of death:
Severe: Yes / No.	Reaction abated after drug stopped or dose reduced:			
	Reaction reappeared after re introduction:			
Was the patient admitted to hospital? If yes, give name and address of hospital				

7. Any laboratory investigations done to evaluate other possibilities? If Yes specify:

8. Whether the patient is suffering with any chronic disorders?
Hepatic Renal Cardiac Diabetes Malnutrition

Any Others

9. H/O previous allergies / Drug reactions:

10. Other illness (please describe):

11. Identification of the reporter:

Type (please tick): Nurse / Doctor / Pharmacist / Health worker / Patient / Attendant / Manufacturer / Distributor / Supplier / Any others (please specify)
Name:
Address:
Telephone / E – mail if any :

Signature of the reporter: **Date:**

Please send the completed form to:

Name & address of the RRC-ASU / PPC-ASU

The Director
National Institute of Siddha,
(Pharmacovigilance Regional Centre For Siddha

Tambaram Sanatorium, Chennai-600 047.
☏ (O) 044-22381314 Fax : 044 –

Website : www.nischennai.org
Email: nischennaisiddha@yahoo.co.in

* ** * * * * *

This filled-in ADR report may be sent within one month of observation /occurrence of ADR

Who Can Report?

⇒ Any Health care professionals like Siddha Doctors / Nurses / Siddha Pharmacists / Patients etc.

What to Report?

⇒ All reactions, Drug interactions,

Confidentiality

⇒ The patient's identity will be held in strict confidence and protected to the fullest extent

Signature of the HOD

CTRI No	CTRI 2016/07/011882
Acknowledgement Number	REF/2016/07/011882
Last Modified On:	22/03/2017
Post Graduate Thesis	Yes
Type of Trial	Interventional
Type of Study	Drug Medical Device Siddha Diagnostic Screening Other (Specify)
Study Design	Other
Public Title of Study Clarification(s) with Reply Modification(s)	Poonaikalivithai chooranam in treatment of Aan maladu(Male infertility)
Scientific Title of Study Clarification(s) with Reply Modification(s)	Clinical study on Aan Maladu(Male infertility) and the drug of choice is Poonaikalivithai chooranam(internal)
Acronym	POONAIKALIVITHAI CHOORANAM
Secondary IDs if Any	**Secondary ID** / **Identifier** NIL / NIL
Details of Principal Investigator or overall Trial Coordinator (multi-center study) Clarification(s) with Reply Modification(s)	**Name**: Dr K RAJENDRAN **Designation**: PG SCHOLAR **Affliation**: NATIONAL INSTITUTE OF SIDDHA **Address**: NATIONAL INSTITUTE OF SIDDHA DEPT OF MARUTHUVAM TAMBARAM SANATORIUM KANCHEEPURAM 600047 NATIONAL INSTITUTE OF SIDDHA DEPT OF MARUTHUVAM TAMBARAM SANATORIUM KANCHEEPURAM 600047 Kancheepuram TAMIL NADU 600047 India **Phone**: 8807565295 **Fax**: **Email**: drrajendrankrish@gmail.com

Details Contact Person Scientific Query Clarification(s) with Reply Modification(s)	**Name**	DR PERIYASAMY PANDIAN
	Designation	ASSOSIATE PROFESSOR
	Affliation	NATIONAL INSTITUTE OF SIDDHA
	Address	DEPT OF MARUTHUVAM NATIONAL INSTITUTE SIDDHA TAMBARAM SANATORIUM KANCHEEPURAM 600047 DEPT OF MARUTHUVAM NATIONAL INSTITUTE SIDDHA TAMBARAM SANATORIUM KANCHEEPURAM 600047 Kancheepuram TAMIL NADU 600047 India
	Phone	9884878469
	Fax	044-22381314
	Email	periasamypandian22@gmail.com
Details Contact Person Public Query Clarification(s) with Reply Modification(s)	**Name**	DR LAKSHMIKANTHAM
	Designation	LECTURER
	Affliation	NATIONAL INSTITUTE OF SIDDHA
	Address	DEPT OF MARUTHUVAM NATIONAL INSTITUTE SIDDHA TAMBARAM SANATORIUM KANCHEEPURAM 600047 DEPT OF MARUTHUVAM NATIONAL INSTITUTE SIDDHA TAMBARAM SANATORIUM KANCHEEPURAM 600047 Kancheepuram TAMIL NADU 600047 India
	Phone	9444466880
	Fax	044-22381314
	Email	drlakshmiramaswamy@gmail.com
Source of Monetary or Material Support Clarification(s) with Reply	AYOTHIDOSS PANDITHAR HOSPITAL	
Primary Sponsor Clarification(s) with Reply	**Name**	AYOTHIDOSS PANDITHAR HOSPITAL
	Address	NATIONAL INSTITUTE SIDDHA TAMBARAM SANATORIUM KANCHEEPURAM
	Type of Sponsor	Research institution and hospital
Details of	**Name**	**Address**

Secondary Sponsor	NIL | NIL
Countries of Recruitment	India
Sites of Study Clarification(s) with Reply	No of Sites = **1** **Name of Principal Investigator** | **Name of Site** | **Site Address** | **Phone/Fax/Email** DR K RAJENDRAN | DR K RAJENDRAN | DEPT OF MARUTHUVAM NATIONAL INSTITUTE SIDDHA TAMBARAM SANATORIUM KANCHEEPURAM 600047 Kancheepuram TAMIL NADU | 8807565295 drrajendrankrish@gmail.com
Details of Ethics Committee Clarification(s) with Reply	No of Ethics Committees= **1** **Name of Committee** | **Approval Status** | **Date of Approval** | **Approval Document** | **Is IEC?** INSTITUTINAL ETHICAL COMMITTEE | Approved | 26/08/2015 | Approval File | No
Regulatory Clearance Status from DCGI	**Status** | **Date** | **Aproval Document** Not Applicable | No Date Specified | No File Uploaded
Health Condition / Problems Studied Clarification(s) with Reply	**Health Type** | **Condition** Patients | AAN MALADU(Male Infertility)
Intervention / Comparator Agent Clarification(s) with Reply	**Type** | **Name** | **Details** Comparator Agent | NIL | NIL Intervention | POONAIKALIVITHAI CHOORANAM(MALE INFERTILITY) | 6g of poonaikalivithai chooranam twice a day orally a period of 48days

<table>
<tr><td>Inclusion Criteria</td><td>
<table>
<tr><td>Age From</td><td>21.00 Year(s)</td></tr>
<tr><td>Age To</td><td>45.00 Year(s)</td></tr>
<tr><td>Gender</td><td>Male</td></tr>
<tr><td>Details</td><td>1.Male infertile
2.Age 21-45 year
3.Maritial status-more than 1 year
4.Sperm count ≤ 40 million/ejaculation
5.Motility less than ≤ 50%
6.Patient who willing to sign the informed consent stating that he will continuously stick to the treatment during 48days but can opt out of the trial of his own conscious discretion
Patients who are willing to give specimen of blood ,urine and semen before and after treatment.</td></tr>
</table>
</td></tr>
<tr><td>Exclusion Criteria</td><td>
<table>
<tr><td>Details</td><td>1.Azoospermia
2.Hydrocele
3.Diabetes mellitus
4.Hypertension
5.Endocrine disorder
6.Cardiac disease
7.VDRL & STD
8.Inguinal Hernia
9.Renal disease
10.Varicose veins</td></tr>
</table>
</td></tr>
<tr><td>Method of Generating Random Sequence</td><td>Not Applicable</td></tr>
<tr><td>Method of Concealment</td><td>Case Record Numbers</td></tr>
<tr><td>Blinding/Masking</td><td>Open Label</td></tr>
<tr><td>Primary Outcome
Clarification(s) with Reply</td><td>
<table>
<tr><th>Outcome</th><th>TimePoints</th></tr>
<tr><td>Primary Outcome is mainly assessed by increase in the sperm count and motility %</td><td>Primary Outcome is mainly assessed by increase in the sperm count and motility %</td></tr>
</table>
</td></tr>
<tr><td>Secondary Outcome
Clarification(s) with Reply</td><td>
<table>
<tr><th>Outcome</th><th>TimePoints</th></tr>
<tr><td>Secondary Out Come is mainly assessed by reduce the clinical symptoms.</td><td>Secondary Out Come is mainly assessed by reduce the clinical symptoms.</td></tr>
</table>
</td></tr>
<tr><td>Target Sample Size</td><td>Total Sample Size="40"
Sample Size from India="40"</td></tr>
</table>

Phase of Trial	Phase 3
Date of First Enrollment (India) Clarification(s) with Reply Modification(s)	16/05/2016
Date of First Enrollment (Global)	No Date Specified
Estimated Duration of Trial	**Years=**"0" **Months=**"6" **Days=**"0"
Recruitment Status of Trial (Global) Clarification(s) with Reply Modification(s)	Not Applicable
Recruitment Status of Trial (India)	Open to Recruitment
Publication Details	NONE YET
Brief Summary	It is single non-ranomized, open-label trial to determine the efficacy of POONAIKALIVITHAI CHIIRANAM(prepared from herbal) in patients with Aan Maladu(MALE INFERTILITY).In this trial 40 patients will be recruited and the trial drug will be administered 6g twice a day for a period of 48days. During the trial period if any AE/SAE/SUSAR will be noticed and refered to pharmacovigilance dept in NIS and further management will also be given in NIS OPD/IPD.The entire trial will be monitored by the research monitoring committee of NIS. During this trial all the safety efficacy parameters will be recorded in the CRF. After completion of the trial all the study related data will be analysed statistically.The outcome of this trial will be published in Indian journal of Medical Research.

The Tamil Nadu Dr.M.G.R.Medical University

69,Anna Salai,Guindy,Chennai - 600 032.

This Certificate is awarded to Dr/Mr/Mrs.....K.....Rajendran.....

for participating as ~~Resource~~ ~~Person~~ / Delegate in the Nineteenth Workshop on

" RESEARCH METHODOLOGY & BIOSTATISTICS "

For ***AYUSH Post Graduates & Researchers***

Organized by the Department of Siddha

The Tamil Nadu Dr. M.G.R. Medical University from 07 th to 11 th September 2015.

Dr.N.KABILAN, M.D.(Siddha)
READER,DEPT.OF SIDDHA

Prof. **Dr.P.ARUMUGAM,** M.D.,
REGISTRAR I/C

Prof. **Dr.D.SHANTHARAM,** M.D., D.Diab.,
VICE CHANCELLOR

NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 600047

BOTANICAL CERTIFICATE

Certified that the following plant drugs used in the Siddha formulation **"Poonaikali vithai Chooranam"** (Internal) for Aanmaladu (Male infertility) taken up for Post Graduation Dissertation studies by **Dr.K.Rajendran**, M.D.(S), II year, Department of Maruthuvam, 2016, are identified through Visual inspection, Experience, Education & Training, Organoleptic characters, Morphology, Micromorphology and Taxonomical methods as

Mucuna prurita Hook. (Fabaceae), Seed

Tribulus terrestris Linn. (Zygophyllaceae), Dried fruit

Asparagus racemosus Willd. (Liliaceae), Root

Bombax malabaricum DC. (Bombacacee), Root

Phyllanthus emblica Linn. (Euphorbiaceae), Root

Tinospora cordifolia (Willd.) Meirs (Menispermaceae), Stem

Saccharum officinarum Linn. (Poaceae), Powder of sugar candy crystal.

MEDICINAL BOTANY CHENNAI 600 047 National Institute of Siddha

Certificate No: NISMB2292016

Date: 28-5-2016

Authorized Signatory

Dr. D. ARAVIND, M.D.(s),M.Sc.,
Assistant Professor
Department of Medicinal Botany
National Institute of Siddha
Chennai - 600 047, INDIA

NATIONAL INSTITUTE OF SIDDHA

राष्ट्रीय सिद्ध संस्थान

Department of AYUSH- MINISTRY OF HEALTH & FAMILY WELFARE

आयुष विभाग - स्वास्थ एवं परिवार कल्याण मंत्रालय

GOVERNMENT OF INDIA-भारत सरकार

TAMBARAM SANATORIUM, CHENNAI -600 047 -ताम्बरम सनटोरियम चेन्नई -600 047

फ़ोन\Tele : 044-22411611 फैक्स\Fax : 22381314

ईमेल: nischennaisiddha@yahoo.co.in वेब :www.nischennai.org

F.No.NIS/6-20/IEC/15-16 Dt: 05.10.2015

CERTIFICATE

Address of Ethics Committee: National Institute of Siddha, Tambaram Sanatorium, Chennai-600047, Tamil Nadu, India	
Principal Investigator: Dr.K.Rajendran, Department of Maruthuvam	
Protocol title: Preclinical and clinical study on AAN MALADU with POONAIKALIVITHAI CHOORNAM.	
Documents filed	1) Protocol, 2) Data Collection forms 3) SAE(Pharmacovigilance)
Clinical trial Protocol (others – Specify)	**Yes**
Informed consent documents	**Yes**
Any other documents	-
Date of IEC approval & its number	**NIS/IEC/9/2014-15/7 – 26.08.2015**

We approve the trial to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study.

Chairman

Member Secretary

C.L.BAID METHA COLLEGE OF PHARMACY

(An ISO 9001-2000 certified institute)

Jyothi Nagar, Old Mahabalipuram Road

Thoraipakkam, Chennai – 600 097

CERTIFICATE

This is to certify that the project entitled, **Toxicological study of POONAIKALI VITHAI CHOORANAM** in rats submitted in partial fulfilment for the degree of **M.D. (siddha)** was carried out at C.L. Baid Metha college of Pharmacy, Chennai-97, in the Department of Pharmacology during the academic year of 2015-2016. It has been approved by the **IAEC No: IAEC/XLIX/13/CLBMCP/2016**

C.L. Baid Metha College of Pharmacy CHENNAI-97 Thoraipakkam

(Dr.P.Muralidharan)

IAEC Member Secretary

BIBLIOGRAPHY

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